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# *ANTIDROMIC RESPONSES FROM THE MELANOPHORE NERVES OF THE CATFISH AMEIURUS*

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Communicated October 29, 1937

In a recent paper (Parker, 1937a) I have shown that the melanophore nerves in the common killifish, Fundulus heteroclitus, exhibit antidromic responses in that on stimulating these nerves, melanophores react in regions proximal to the point of stimulation as well as distal to it. I have also pointed out that one reason why this condition had not already been reported was that the melanophores proximal to the point from which the experimental band had been excited were under antagonizing influences which kept them from responding in an obvious way as did those distal to this point where these influences were necessarily absent. Since these observations were made I have been enabled to test this question on another bony fish, the common hornpout Ameiurus nebulosus.

The tests on this fish were carried out in essentially the same way as those on Fundulus and with corresponding results. When a dark band produced by a cut in the tail of a pale Ameiurus is allowed to blanch for a day or two, it can be reactivated by making a new cut midway on its length, whereupon its melanophores will disperse their pigment in positions not only distal to the new cut but also proximal to it. This dispersion of pigment passes proximally beyond the first cut (that by which the original band was excited) only to a very limited degree, but it is clearly and obviously present up to that point. It must result from antidromic responses passing in a proximal direction from the new cut over the dispersing melanophore nerve fibres which of course also at the same time transmit responses distally from this cut.

In a similar way a newly induced but partly faded caudal band in Ameiurus can be made to fade very fully by applying to it near the midpoint on its length an electric stimulus from an inductorium. The fading in this instance like the darkening in the preceding one extends both proximally and distally from the point of application of the stimulus, but does not pass

appreciably beyond the cut by which the band was originally excited. This test shows that the concentrating nerve fibres of Ameiurus like its dispersing fibres exhibit antidromic responses. Thus the melanophore nerves of Ameiurus, both dispersing and concentrating, show antidromic activities as the corresponding ones in Fundulus do. It is remarkable that I have been unable thus far to elicit any evidence of antidromic activity from the concentrating fibres of the dogfish Mustelus (Parker, 1937b), a fish whose color responses would lead one to expect a more certain demonstration of this phenomenon than could be looked for in either Fundulus or Ameiurus.

Parker, G. H., "Do Melanophore Nerves Show Antidromic Responses?" *Jour. Gen. Physiol.*, **20**, 851–858 (1937a).

Parker, G. H., *Melanophore Responses in the Young of Mustelus canis* (in press) (1937b).

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## *ANTAGONISM IN NEUROHUMORS AS SEEN IN THE PECTORAL BANDS OF MUSTELUS*

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The smooth dogfish, Mustelus canis, darkens from the action on its melanophores of the pituitary hydrohumor intermedin (Lundstrom and Bard, 1932). It blanches from the effect on the same color cells of a concentrating lipohumor derived from autonomic nerve-fibres (Parker and Porter, 1934). The two substances here involved, intermedin which causes a dispersion of melanophore pigment, and the lipohumor which induces its concentration, are obviously antagonistic, and this antagonism appears to offer an explanation for several features not heretofore clearly understood in the color changes of this fish.

The antagonism just pointed out makes itself evident in certain peculiarities best seen in the band formation that takes place in the pectoral fins of Mustelus when transverse cuts are made in these fins (Figs. 1 and 2). When in a moderately dark Mustelus an appropriate incision is made in its pectoral fin, a pale band forms in ten minutes or so and stretches from the newly made cut nearly to the edge of the fin. Bands such as this show a variety of conditions all of which lie between two extremes. Either the band is of about the width of the cut and with fairly well defined, rectilinear sides thus presenting a simple, clearly circumscribed and regular outline (Fig. 1), or it is relatively narrow and somewhat tortuous in its course, though never passing beyond what would be the limits of the first type of

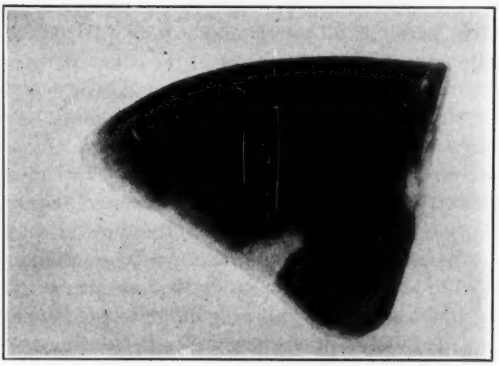

FIGURE 1

Dorsal view of a left pectoral fin from a darkish Mustelus showing a full and regular pale band formed from a transverse cut. The fish was in process of blanching and the band is believed to have resulted from the unimpeded action of the concentrating lipohumor.

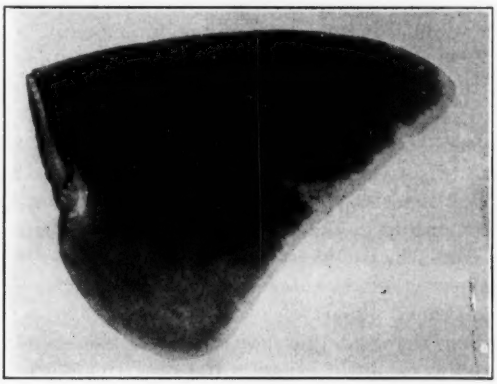

FIGURE 2

Dorsal view of a right pectoral fin of a darkish Mustelus showing a restricted and irregular pale band formed from a transverse cut. The fish was in process of darkening and the band is believed to have resulted from the action of a concentrating lipohumor antagonized by intermedin.

band. The edges of this second type are vague and somewhat hazy and may at times even meet crosswise, thus interrupting the band (Fig. 2). Between these two extremes all intergrades occur.

From the time when I began the study of the color changes in Mustelus, I had been familiar with these two types of bands without, however, appreciating their significance. I had supposed in a general way that they represented differences in the distribution of the nerves in the fins of different individual fishes, but in the course of certain experiments I was surprised to find that both types of bands could be excited on the same fin provided a considerable interval lapsed between the times of the two cuttings. I then recorded the conditions under which each type of band appeared and I was thereby led to see that regular bands were produced in dogfishes that were changing from dark to pale and irregular ones were formed during the reverse change. The occasion of these differences seemed to rest on the following conditions. When a dogfish is in process of darkening, its blood must be rich in intermedin and if under these circumstances a pale band is initiated, the concentrating lipohumor from the severed nerves must work on melanophores which at the same time are subject to the dispersing action of the intermedin in the blood. Under these circumstances the intermedin would antagonize the lipohumor and the resulting pale band would be in consequence only imperfectly formed. Admitting this explanation one would expect the forming pale band to be invaded from the sides where the intermedin would be in full concentration, an expectation that appears to be realized by the actual condition of the band (Fig. 2). This irregular type of band then results from the opposition of the intermedin to the lipohumor concerned.

When a dogfish of a moderately dark tint begins to turn pale, its blood should contain little or no intermedin and the blanching of a band should proceed under the almost exclusive action of the concentrating lipohumor. Under these circumstances the lipohumor would act without opposition and the band should be complete and full as in fact it is (Fig. 1). Here the absence of neurohumoral antagonism would allow the formation of a complete and full band.

The explanations that have thus been offered for these two types of bands admit of a certain amount of experimental test. The blood of a dogfish which is in process of darkening and which in consequence would form only imperfect bands on being tested ought to give evidence of functional amounts of intermedin and that of a fish that was blanching and would form full bands ought to show no signs of this dispersing hormone. Such appears to be true, for when the blood of a darkening fish is injected into a pale one a dark area arises in the region of injection, but no color change results from a like injection into a dark fish. When the blood of a blanching fish is injected into either a dark or a pale one, no color change whatsoever

is to be noticed. These observations then support the opinion that in a darkening fish intermedin and the concentrating lipohumor are in antagonistic relations and in a blanching fish the concentrating lipohumor acts in a wholly unimpeded way.

Another feature of band formation, namely that of the time differences in the production of bands, also appears to result from neurohumoral antagonism. Pale bands both in adult dogfish and in pups, as table 1 shows, form more quickly (6.5 to 9.5 minutes) when the fish is blanching than when it is darkening (13 to 18 minutes). Their differences in times are consistent with the idea of neurohumoral antagonism, for when the neurohumors act in opposition (darkening) the process takes a longer time (13 to 18 minutes) than when the single lipohumor acts without interference (6.5 to 9.5 minutes). Thus these differences in times are reasonable differences from the standpoint of neurohumoral antagonism.

From these observations it seems probable that poorly defined pale bands result from the antagonistic action of intermedin on the concentrating lipohumor and that well defined, full bands are the product of the unimpeded action of the lipohumor alone. Such peculiarities illustrate well the kind of antagonisms to which neurohumors are subject and which must be taken into account in understanding many color changes. Antagonisms such as these are of course not to be sought for in those chromatic vertebrates where, as in the lamprey (Young, 1935), many elasmobranchs

TABLE 1

Times in minutes for the first appearance and the completion of pale bands after cuts have been made in the pectoral fins of pups and of mature dogfishes (Mustelus canis) in the dark condition and the pale condition. In each series of tests six fishes were used. The fishes in these series had been attuned to a dark phase or to a pale one by a preliminary residence in an illuminated black-walled tank or in a white-walled one for about a day and a half.

| | PUPS | | ADULTS | |
|---|---|---|---|---|
| STATE OF BAND | DARKENING | BLANCHING | DARKENING | BLANCHING |
| First Indication | 7.5 to 10.0 | 4.0 to 5.0 | 8.0 to 9.5 | 3.5 to 4.0 |
| Completion | 13.0 to 16.0 | 7.0 to 9.5 | 15.0 to 18.0 | 6.5 to 9.0 |

(Wykes, 1936), the American frog (Parker and Scatterty, 1937) and the lizard Anolis (Kleinholz, 1936), only one neurohumor is present, but in those that have two or more such agents such as Mustelus, certain teleosts, as, for instance, Fundulus and Ameiurus, and certain lizards, Phrynosoma and possibly Chameleo (Parker, 1937). The principle of antagonism here illustrated implies a certain amount of tissue storage and of interaction among neurohumors as has been suggested already for other aspects of melanophore activity (Parker and Brower, 1937).

*Summary.*—1. Pale bands produced by the cutting of bundles of nerves in the pectoral fins of Mustelus canis may be either full and regular in outline or tortuous, restricted and irregular in form.

2. Regular bands occur in dogfishes that are blanching and are excited by a concentrating lipohumor acting unimpeded.

3. Irregular bands occur in dogfishes that are darkening and are the result of the antagonism between the dispersing hydrohumor intermedin and a concentrating lipohumor from the nerves.

4. The blood from a darkening Mustelus shows evidence of containing intermedin to a functional degree; that from a blanching one shows no such evidence.

5. The formation of a pale band by the unopposed action of the lipohumor takes place in less time (6.5 to 9.5 minutes) than it does when this action is opposed by that of intermedin (13 to 18 minutes).

Kleinholz, L. H., "Studies in Reptilian Color Changes," *Proc. Nat. Acad. Sci.*, **22**, 454–456 (1936).

Lundstrom, H. M., and Bard, P., "Hypophysial Control of Cutaneous Pigmentation in an Elasmobranch Fish," *Biol. Bull.*, **62**, 1–9 (1932).

Parker, G. H., "The Color Changes in Lizards, Particularly in Phrynosoma," *Jour. Exptl. Biol.* (in press) (1937).

Parker, G. H., and Brower, H. P., "An Attempt to Fatigue the Melanophore System in Fundulus and a Consideration of Lag in Melanophore Responses," *Jour. Cell. Comp. Physiol.*, **9**, 315–329 (1937).

Parker, G. H., and Porter, H., "The Control of the Dermal Melanophores in Elasmobranch Fishes," *Biol. Bull.*, **66**, 30–37 (1934).

Parker, G. H., and Scatterty, L. E., "The Number of Neurohumors in the Control of Frog Melanophores," *Jour. Cell. Comp. Physiol.*, **9**, 297–314 (1937).

Wykes, U., "Observations on Pigmentary Co-Ordination in Elasmobranchs," *Jour. Exptl. Biol.*, **13**, 460–466 (1936).

Young, J. Z., "The Photoreceptors of Lampreys. II. The Functions of the Pineal Complex," *Jour. Exptl. Biol.*, **12**, 254–270 (1935).

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## *THE FOUR TRANSVERSE MAGNETIC EFFECTS IN COPPER: NEW MEASUREMENTS*

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Communicated November 5, 1937

During the last few years I have been striving, with much physical labor and with a gradually improving technique, to get reasonably accurate measurements of these four effects in copper at various temperatures ranging from about 20°C. to about 90°C.

My aim has been to measure each of the effects with an accuracy of one

per cent at each of three temperatures, and though I have probably fallen somewhat short of this mark, especially with the Ettingshausen effect, I feel that the results arrived at are probably more accurate than those previously obtained in this particular field of research.

Leaving experimental details to be described in the Proceedings of the American Academy of Arts and Sciences, I will give these results at once. $R$ being the Hall effect coefficient, $P$ the Ettingshausen, $Q$ the Nernst and $S$ the Righi-Leduc, I get

TABLE 1

| TEMP. | $R \times 10^4$ | TEMP. | $P \times 10^9$ | TEMP. | $Q \times 10^4$ | TEMP. | $S \times 10^7$ |
|---|---|---|---|---|---|---|---|
| 24° | −5.36 | 22.5° | −1.441 | 24.9° | −2.155 | 24.9° | −2.699 |
| 54.5° | −5.37 | 56.7° | −1.550 | 54.4° | −2.106 | 54.0° | −2.454 |
| 91.5° | −5.38 | 91.4° | −1.703 | 84.1° | −2.017 | 84.2° | −2.275 |

According to these figures the temperature coefficient is for $R$ very small, positive and practically constant within the range of temperature used; for $P$ considerable, positive, not constant; for $Q$ smaller, negative, not quite constant; for $S$ fairly large, negative, not constant. I do not consider my experiments accurate enough to prove variability of any one of the temperature coefficients, but for the purpose of interpolation or extrapolation needed to get values of $R$, $P$, $Q$ and $S$ at the three temperatures 25°, 55°, 85°, I have plotted temperature curves for all the effects except $R$. I thus get the following table of values, which I shall, in view of the small range of interpolation or extrapolation just referred to, count as "observed" values, like those of table 1:

TABLE 2

| TEMP. | $R \times 10^4$ | $P \times 10^9$ | $Q \times 10^4$ | $S \times 10^7$ |
|---|---|---|---|---|
| 25° | −5.36 | −1.446 | −2.155 | −2.698 |
| 55° | −5.37 | −1.544 | −2.104 | −2.448 |
| 85° | −5.38 | −1.674 | −2.014 | −2.272 |

*Application of These Numbers.*—Several years ago I developed and published a theory of electric and thermal conduction in metals. According to this theory I should be able, when any two of the four transverse effects are known in sign and magnitude for any metal at a given temperature, and when certain other information concerning the electric and thermal properties of the metal is available, to calculate in advance of experiment the sign and magnitude of each of the other transverse effects in the same metal at the same temperature. I shall not here make any formal argument in favor of this theory nor shall I even restate it. I shall merely undertake to find how good a practical rule it affords me for calculating the values of the Nernst and Righi-Leduc effects from the values of the

Hall and Ettingshausen effects, with the somewhat imperfect data I now have at hand.

In making this test I shall use especially certain equations taken from my paper published in the *Proceedings of the National Academy of Sciences* for July, 1925, and the table of "characteristic constants" given in my *N. A. S.* paper of January, 1930. The numbers attached in square brackets to the equations used are those which these equations had in the original paper. The equations are

$$R = (R_a\kappa_a + R_f\kappa_f) \div \kappa, \qquad (1) \qquad [2]$$

where $R$ is the Hall effect coefficient, $\kappa$ is the total specific electric conductivity (absolute) of the metal, and the subscripts $a$ and $f$ refer to the "associated" and the "free" electrons of the metal, respectively; $\kappa = \kappa_a + \kappa_f$, and $(\kappa_f \div \kappa) = C + C_1t + C_2t^2$, where $t$ is the temperature and $C$, $C_1$ and $C_2$ have values given in table 1 of the 1930 paper.

$$P = (R - R_f)\kappa_f(\lambda \div \theta), \qquad (2) \qquad [3]$$

where $P$ is the Ettingshausen coefficient, $\lambda$ is the number of ergs required to "free" $(1 \div e)$ electrons $(6.284 \times 10^{19}$ electrons) *within* the metal, and $\theta$ is the thermal conductivity of the metal when heat is expressed in ergs. According to my theory the number of ergs required to free a single electron *within* the metal is $\lambda'_c + skT$, where $T$ is the absolute temperature, $k$ is the Boltzmann gas-constant, $1.37 \times 10^{-16}$, and $\lambda'_c$ and $s$ have values given in the table of "characteristic constants" already referred to. The other equations are

$$Q_f = -R_f(\theta \div \lambda)(\kappa \div \kappa_f), \qquad (3) \qquad [7]$$

where $Q_f$ is the part of the Nernst effect due to the free electrons,

$$Q = R_a - R_f)(\theta \div \lambda), \qquad (4) \qquad [9]$$

$Q$ being the total Nernst coefficient, and

$$S = (Q - Q_f)\kappa_f(\lambda \div \theta) \qquad (5) \qquad [10]$$

where $S$ is the Righi-Leduc coefficient.

I shall use the temperatures 25°, 55° and 85°, getting values of $R$, $P$, $Q$ and $S$ for these temperatures from table 2 of this paper. The values of the electrical and the thermal conductivities for the chosen temperatures are found by interpolation from those given for 0° and 100° in table 2 of my 1930 paper. I thus have

TABLE 3

| TEMP. | $\kappa \times 10^6$ | $\kappa_f \times 10^6$ | $\kappa_a \times 10^6$ | $\lambda + \theta$ |
|---|---|---|---|---|
| 25° | 581.0 | 42.6 | 538.4 | 0.429 |
| 55° | 520.2 | 37.8 | 482.4 | 0.475 |
| 85° | 471.3 | 34.0 | 437.3 | 0.521 |

Using the data of table 3, and the $R$ and $P$ values of table 2, in equations (1) to (5) I get "calculated" values for $Q$ and $S$ at the three temperatures mentioned. Comparison of these calculated values with the observed values of $Q$ and $S$ is made in table 4.

TABLE 4

| TEMP. | $R \times 10^4$ Obs. | $P \times 10^9$ Obs. | $Q \times 10^4$ Obs. | $Q \times 10^4$ Calc. | $S \times 10^7$ Obs. | $S \times 10^7$ Calc. |
|---|---|---|---|---|---|---|
| 25°C. | −5.36 | −1.446 | −2.155 | −1.958 | −2.698 | −2.694 |
| 55°C. | −5.37 | −1.544 | −2.104 | −1.958 | −2.448 | −2.383 |
| 85°C. | −5.38 | −1.674 | −2.014 | −1.915 | −2.272 | −2.124 |

The ratios of the observed to the calculated values are, for $Q$, 1.10, 1.07, 1.05, and for $S$ they are 1.00, 1.03 and 1.07. In every case the calculated value has the right sign, and for both $Q$ and $S$ the direction of the change with rise of temperature is correctly indicated.

Certain moderate changes in the observed values of $P$, the most uncertainly measured of all the four effects, would make the agreement between the calculated and the observed values of $Q$ and $S$ better. Possibly such changes would be found in measurements of $P$ under improved conditions, but that is a matter of conjecture. Rather than spend more time on copper at present I prefer to work now with another metal, palladium, in which the Ettingshausen effect is much larger, though the Righi-Leduc may be smaller, than in copper.

It is to be remembered that the values of $\kappa_f$, $\kappa_a$ and $\lambda$ used in the preceding calculations are derived from a collection of material (table 1 of my January, 1930, paper) to which the four transverse effects contributed nothing. Until I had made such a test I had no means of knowing, except from my general theory of dual conduction in metals, whether these values, when used in my equations connecting the various transverse effects, would enable me to get, from the observed values of $R$ and $P$, values for $Q$ and $S$ even remotely resembling their observed values. The comparatively good agreement which I have found in this test encourages me to believe that the quantities, $\kappa_f$, $\kappa_a$ and $\lambda$ have a genuine significance and that the numerical values I have found for them by use of my table of "characteristic constants" are not very different from their true values.

Let us discuss, for example, $\kappa_f$ and $\kappa_a$. From considerations having no connection, no obvious or reckoned-upon connection, with the transverse effects I long ago reached the conclusion that $\kappa_f$ is in copper much smaller than $\kappa_a$, and in my calculations for getting values of $Q$ and $S$ I have taken it to be so. If in these calculations I take $\kappa_f = \kappa_a$, each being one half of $\kappa$, other data remaining unchanged, I get by calculation $Q = -0.559 \times 10^4$ at 25°C. instead of the observed value $-2.155 \times 10^{-4}$. Using the values of $\kappa_f$ and $\kappa_a$ that my table of "characteristic constants" gave I got by calculation $Q = -1.958. \times 10^{-4}$.

# ON THE MAGNETIC ENERGY OF SUPRACONDUCTORS

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Communicated November 1, 1937

1. A long stretched supraconductive body (wire), placed longitudinally in a homogeneous magnetic field of slowly increasing strength $H_0$ loses its supraconductivity when the field strength reaches a certain critical value $H_0 = H_c$. Measurements by de Haas and Voogd[1] disclosed that the case is different when the direction of the wire is transverse: then the transition takes place at a value of the applied field $H_0$ lower than $H_c$. By $H_0$ is meant the field as it would be if the supraconductor were absent. When it is present, the strength $H$ is in general different from $H_0$ and varies from point to point, because the field cannot penetrate into the supraconductive material, so that the lines of induction are crowded at its surface. These conditions caused Von Laue[2] to enunciate the following hypothesis: *A supraconductive body begins its transition into the normal state when the strongest part of the magnetic field H at its surface reaches the critical value* $H = H_c$. Subsequent measurements by de Haas and co-workers on circular and elliptic cylinders[3] and on spheres[4] confirmed Von Laue's rule, so that it must be regarded as firmly established experimentally. Recently it has gained added theoretical importance, having been made by Landau[5] the starting point of interesting considerations on the structure of supraconductors during the process of transition.

The theoretical reasons for the dependence of the critical field $H_c$ on the temperature were cleared up in a significant paper by Gorter and Casimir,[6] in which these authors also attempted a theoretical derivation of Von Laue's rule. However, this part of their work is, in our opinion, unconvincing and open to certain objections. In view of the great importance of the subject it seemed desirable to study it more closely in order to remove all doubts which may arise. The purpose of the present paper is to supply this want and to modify the derivation of Von Laue's rule in such a way as to meet the objections.

2. It is usually said that a supraconductive wire in a longitudinal homogeneous magnetic field does not appreciably change the field distribution.[7] The strength of field retains the value $H_0$ everywhere, except in the interior of the wire where it vanishes. When the wire (whose volume we denote by $V$) loses its supraconductivity, the increase of magnetic energy of the system is, therefore, $\Delta W_M = VH_0^2/8\pi$, i.e., equal to the field energy contained in its volume after the field has penetrated into it.

Let us now consider the general case of a supraconductor of any shape in an inhomogeneous field (Fig. 1); let its surface be initially $ABCDE$; and

let the (tangential) field at the point $C$ be denoted by $H$. Suppose that an infinitesimal volume element at the surface, $BCDFB$, loses its supraconductivity so that the volume of the body changes by the negative value $\Delta V$. If it were possible to prove that the attendant increase of magnetic energy is

$$\Delta W_M = -\frac{H^2}{8\pi}\Delta V, \tag{1}$$

then the same mathematical relations would obtain in the *general* conditions of any local supraconductive change as in the *special* conditions of the wire in a longitudinal field: if the law $H_o = H_c$ obtains in the latter process, it should be $H = H_c$ in the former. In other words, the validity of the formula (1) implies the validity of Von Laue's rule.

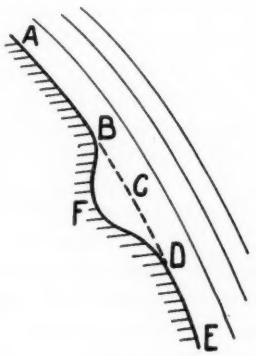


FIGURE 1

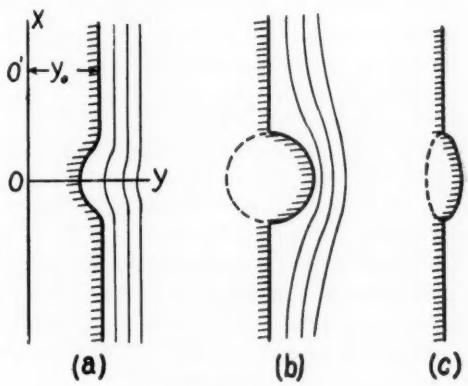


FIGURE 2

In their attempt to derive equation (1) Gorter and Casimir start from the case of a supraconductive half space with an indentation of infinitesimal volume in it. The other half space is filled with a homogeneous magnetic field, distorted at the indentation, and extending into infinity (Fig. 2a). We are unable to follow their argument nor can we confirm their results. We propose to show here (*a*) that the model of the infinite homogeneous field is inadequate for the purpose, giving a result three times too small; (*b*) that the validity of the formula (1) is not general.

If equation (1) is correct, it should apply also to positive $\Delta V$, i.e., to humps as well as depressions. We may, therefore, begin with the case of a half spherical or a half ellipsoidal hump in a plane. Mathematically the problem is the same as that of a complete sphere or ellipsoid (dotted lines) in a homogeneous field, endless in all directions. It will be well to general-

ize the problem in two respects: (1) we shall consider a homogeneous body of any shape in an initially homogeneous field, (2) we attribute to it any magnetic permeability $\mu$. If we characterize the interior and exterior of the body by the indices $i$ and $e$ (Fig. 3), the total field energy within a sphere of the large radius $R$ is

$$W_M = \frac{1}{8\pi}\left[\mu \int H_i^2 d\tau + \int_e H_e^2 d\tau\right]. \tag{2}$$

Since $H$ can be derived from a potential, $H = -\nabla\Phi$, we find by means of Green's theorem

$$W_M = \frac{1}{8\pi}\left[\mu \int_{S_i} \Phi_i \frac{\partial \Phi_i}{\partial N} ds - \int_{S_i} \Phi_e \frac{\partial \Phi_e}{\partial N} ds + \int_{S_R} \Phi_e \frac{\partial \Phi_e}{\partial N} ds\right]. \tag{3}$$

The conditions at the surface $S_i$ are

$$\Phi_i = \Phi_e, \qquad \mu \frac{\partial \Phi_i}{\partial N} = \frac{\partial \Phi_e}{\partial N}.$$

Hence, the two first terms of (2) cancel out (in all cases, except $\mu = \infty$), and the energy becomes

$$W_M = \frac{1}{8\pi} \int_{S_R} \Phi_e \frac{\partial \Phi_e}{\partial R} ds. \tag{4}$$

The potential $\Phi_e$ consists of two parts, $\Phi_e = \Phi_o + \Phi_p$, where $\Phi_o$ is the contribution of the original homogeneous field and $\Phi_p$ the perturbation due to the presence of the body. The expression for the first term is in polar coördinates $\Phi_o = -H_o r \cos\vartheta$, whereas $\Phi_p$ can be expanded into a series of spherical harmonics

$$\Phi_e = -H_o\left[r\cos\vartheta + A\frac{\cos\gamma}{r^2} + B\frac{K_2(\vartheta,\varphi)}{r^3} + \ldots\right], \tag{5}$$

where $\vartheta$ denotes the angle between $H_o$ and the radius vector, and $\gamma$ between the direction of the dipole $(\vartheta_o, \varphi_o)$ and the radius vector, $\cos\gamma = \cos\vartheta_o\cos\vartheta + \sin\vartheta_o\sin\vartheta\cos(\varphi - \varphi_o)$.

Substituting into (3) we notice that, for $R \to \infty$, only the first and second term give a contribution to the integral, since the element of surface $ds$ is proportional to $R^2$.

$$W_M = \frac{H_o^2}{8\pi}\left[\frac{4\pi}{3}R^3 + \frac{4\pi}{3}A_H\right], \tag{6}$$

where $A_H = A\cos\vartheta_o$ is the component of the dipole in the direction of the field. The first term represents the energy in the absence of the body, $W_o$. In formula (1) the energy change is defined as $\Delta W_M = W_o - W_M$

i.e., the change that takes place when the body is removed. Since $A_H$ is always proportional to the volume of the body, $4\pi A_H/3 = \alpha\Delta V$, we may write

$$\Delta W_M = (H_o^2/8\pi)\cdot(4\pi A_H/3), \tag{7}$$

$$\Delta W_M = -\alpha\frac{H_o^2}{8\pi}\Delta V, \tag{8}$$

where the coefficient $\alpha$ depends on the shape of the body.

The values of $A_H$ and, consequently, of $\alpha$ may be found in any textbook of electricity. In the case of a sphere, $\alpha = (1-\mu)/(\mu+2)$; for a very flat ellipsoid, $\alpha = (1-\mu)/3$. The last expression applies to any triaxial ellipsoid such that the axis oriented in the direction of the field is very large compared with one (or both) of the other axes. The particular conditions applying to supraconductors are obtained by putting $\mu = 0$, which gives for $\alpha$ in the two cases considered $^1/_2$ and $^1/_3$. As was mentioned above these results apply also to humps of corresponding shapes in a plane surface (Fig. 2b, c). In neither case does the calculated expression agree with formula (1).

To remove all doubts that the same conclusions apply also to very flat depressions as well as humps, we consider still one more case. Let us imagine a magnetic dipole placed in the point $O$ of figure 2a, having the strength $A = -\kappa$ and direction $OO'$. This dipole will cause a distortion of the homogeneous field and bend the lines of force, in the plane $AB$ into a shape indicated in the figure. We shall take the locus geometricus of the bent lines as the surface of the supraconductor and calculate the volume of the indentation and the energy due to it. The potential to the right of the surface $AB$ is

$$\Phi = -H_o(r - \kappa/r^2)\cos\vartheta, \tag{9}$$

which is of the general form (5). However, the integral (4) must be extended only over the half space outside the body and not over the whole space. We have therefore to supply formula (7) with the factor $^1/_2$. Hence $\Delta W_M = (H_o^2/8\pi)\cdot(2\pi\kappa/3)$.

From the expression (9) of the potential it is not hard to calculate the equation of the surface $AB$. It turns out to have the form

$$y(1 + 2\kappa/r^3) = y_o.$$

The depression is shallow when $\kappa/y_o^3$ is small compared with 1. Making this assumption we neglect squares of this number and find for the change of volume due to the indentation $\Delta V = -2\pi\kappa$. This gives for $\Delta W_M$ the formula (8) with $\alpha = ^1/_3$, just as in the case of the flat hump. We can therefore summarize our results for supraconductors as follows:

| | |
|---|---|
| Semi-spherical hump | $\alpha = 1/2$ |
| Flat hump or shallow depression with border line of any shape | $\alpha = 1/3$ |

3. The above results are, however, in contradiction with the method of calculating the magnetic energy change of a field from the magnetic moment produced by it. If the undisturbed field is appreciably homogeneous over the space later occupied by the body, the magnetic moment produced by it has a simple connection with the "strength of the dipole" $A$ in formula (5), namely $M = H_0 A$. The energy $-\Delta W_M$ of producing this dipole is according to the theory of electricity

$$-\Delta W_M = \int \mathbf{H}_0 \cdot \mathbf{dM} = \frac{1}{2} H_0 M \cos(M, H_0), \tag{10}$$

$$\Delta W_M = -\frac{H_0^2}{8\pi} 4\pi A_H, \tag{11}$$

or exactly three times as much as given by formula (6).

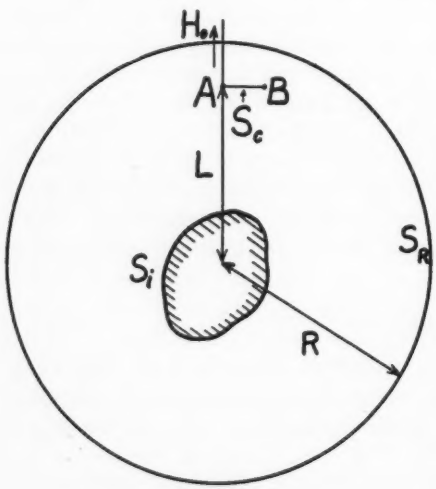

FIGURE 3

The discrepancy must be due to the inadequacy of the infinite homogeneous field. Such a field does not exist in nature and is only a *model*, an artificial device for making the problem definite. To resolve the contradiction we shall replace this model by one closer to reality. A magnetic field can be produced only by moving charges or *currents*. We shall prove that the *energy of a field originating in currents always obeys the formula* (11). We start from the simplest case of a closed linear current $AB$ of the total current $J$ and the very small plane area $S_c$, normal to the line $AO$ connecting it with the body to be magnetized (Fig. 3). Since we wish the field produced by it to have the nearly constant value $H_0$ over the extent of the body $S_i$ we assume the distance $L$ between $A$ and $O$ to be very large compared with the size of the body.

The potential of a linear current has at the point $Q$ the expression $\Phi_c = J\omega_Q$, where $\omega_Q$ is the solid angle subtended by the current to the point

$Q$. This becomes in the very distant point $R = 0$, $\Phi_c = JS_c/L^3$, whence the strength of field $H_o = -\partial\Phi_c/\partial L = 2JS_c/L^3$. We find, therefore,

$$JS_c = \frac{1}{2}H_oL^3. \tag{12}$$

Turning back to the transformation of the integrals (2) we notice that we can no longer apply Green's theorem to the space within the sphere of radius $R$ (Fig. 3) because the potential $\Phi_c$ is many valued. To remove the many-valuedness we must lay a "branch cut" $AB$ through the current (coinciding with what we called its *area* $S_c$). The space receives in this way two new border surfaces, the upper and lower sides of the cut $AB$, which we shall characterize by the second subscripts 2 and 1. The application of formula (3) is now permissible provided the integral is extended over the new borders. On the other hand, the integral over the infinite sphere vanishes, because the potential $\Phi = \Phi_c + \Phi_p$ decreases in infinity proportionally to $1/R^2$. We find, therefore, instead of equation (4)

$$W_M = -\frac{1}{8\pi}\int_{S_c}\left\{(\Phi_{c2}+\Phi_{p2})\left(\frac{\partial\Phi_{c2}}{\partial N}+\frac{\partial\Phi_{p2}}{\partial N}\right)-(\Phi_{c1}+\Phi_{p1})\left(\frac{\partial\Phi_{c1}}{\partial N}-\frac{\partial\Phi_{p1}}{\partial N}\right)\right\}ds.$$

The energy $W_o$ in the absence of the body is obtained from this expression by putting $\Phi_p = 0$. Moreover, the potential $\Phi_p$ as well as both the strengths $\partial\Phi_c/\partial N$ and $\partial\Phi_p/\partial N$ are *not* many valued being the same for both subscripts. Therefore

$$\Delta W_M = W_o - W_M = \frac{1}{8\pi}\int_{S_c}(\Phi_{c2}-\Phi_{c1})\frac{\partial\Phi_p}{\partial L}\,ds. \tag{13}$$

According to the above expression for $\Phi_c$ the difference $\Phi_{c2} - \Phi_{c1} = J(\omega_2-\omega_1) = 4\pi J = 2\pi H_oL^3/S_c$. In view of the largeness of $L$ only the second term of (5) gives an appreciable contribution to the factor $\partial\Phi_p/\partial L$, namely $-2H_oA\cos\gamma$. Since $\gamma = \vartheta_o$ is here the angle between the field $H_o$ and the dipole, we have $A\cos\gamma = A_H$ and

$$\Delta W_M = \frac{H_o^2}{8\pi}4\pi A_H \tag{14}$$

in complete agreement with the expression (11).

The generalization of this result for any distribution of currents is a trivial matter and we shall only briefly indicate here the necessary steps. The most important step is to show that the result (14) is also true when the plane of the tiny closed current is not normal to the line $OA$ but has any orientation. According to the Ampere-Stokes theorem, any closed current

can be represented as a superposition of infinitesimal closed currents; this permits the immediate generalization for any current sufficiently far away from the body. Moreover, the magnetic moments are additive (the magnetic moment of any body is the sum of the magnetic moments of its parts). Therefore, restriction to wide currents may be removed by mentally breaking up the magnetized body into infinitesimal units.

It goes without saying that, when the body $S_i$ and the current form a closed system, any energy increase of the body takes place at the expense of the energy of the current: the magnetization created in the body reacts upon the current in such a way that the total field energy remains unchanged.[8] This obvious fact is, however, irrelevant for our computation because we are interested in *the work done by outer forces against the body* $S_i$. The current is for us an external agency used to produce the magnetization in $S_i$; it is, therefore, best to imagine $J$ maintained constant by external energy supplies.

We recall that the purpose of our investigation is to find whether the formula (1) is valid. In this connection our result that the factor of equation (8) must be multiplied by 3 compared with the values given at the end of section 2. We find, therefore, for supraconductors

| | |
|---|---|
| Spherical hump in plane | $\alpha = {}^3/_2$ |
| Flat hump or shallow depression of any border line | $\alpha = 1$ |

We see that the contention expressed in formula (1) *has no general validity but applies only to shallow depressions* (or flat humps). This is, however, quite sufficient to explain Von Laue's rule in supraconductive transitions: since the regions where the state is normal gradually penetrate into the supraconductor from its surface they must be necessarily shallow in the beginning of the process.

[1] de Haas and Voogd, *Comm. Leiden*, **214c** (1931).

[2] M. Von Laue, *Phys. Zeits.*, **33**, 793 (1932).

[3] de Haas, Voogd and Jonker, *Physica*, **1**, 280 (1934); de Haas and Casimir-Jonker, *Physica*, **1**, 291 (1934).

[4] de Haas and Guineau, *Physica*, **3**, 182, 534 (1935).

[5] L. Landau, *Phys. Zeit. Sowjetunion*, **11**, 129 (1937).

[6] Gorter and Casimir, *Physica*, **1**, 306 (1934).

[7] The correctness of this assertion follows from the discussion in section 3.

[8] Compare: H. A. Lorentz, *Marx's Handbuch der Radiologie*, Vol. VI, p. 141, Leipzig 1925; also: P. S. Epstein, *Proc. Nat. Acad. Sci.*, **12**, 634 (1926). The magnetization induced in the body $S_i$ is also due to molecular or macroscopic currents, and its magnetic moment can be replaced by an induced closed current $J_p$. When this is done, two new terms in $\Delta W_M$ arise. (A) An integral of the same form as (13), but with the subscripts $c$ and $p$ interchanged, extended over $S_p$. This integral represents the mutual energy of the field and of the magnetic moment induced by it. It is identical with the expression (10). Both this term and (13) take then a form symmetrical in $c$ and $p$, so that their numerical equality becomes directly evident. (B) The second arising term is the energy of the induced current itself, which must be oppositely equal to the first term, because of conservation of energy.

# ACID CATALYSIS IN LIQUID AMMONIA. I. AMMONOLYSIS OF DIETHYLMALONATE

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Numerous investigations have shown that liquid ammonia possesses unusual properties as a solvent[1] for many inorganic and organic compounds. Like water it is the parent substance of a system of acids, bases and salts.[2] Liquid ammonia also reacts directly with many substances. Solvolysis takes place and in the case of ammonia such reactions are termed *ammonolytic* reactions. Just as phosphorus trichloride is hydrolyzed by water (1), so it may be ammonolyzed[3] by ammonia to give the nitrogen analogs of phosphorous and hydrochloric acids (2).

$$PCl + 3HOH \rightarrow P(OH)_3 + 3HCl \quad (1)$$

$$PCl_3 + 5HNH_2 \rightarrow P(NH)(NH_2) + 3NH_4Cl \quad (2)$$

Many hydrolytic reactions are catalyzed in aqueous solutions by acids or bases. Thus, the inversion of cane sugar is catalyzed by acids and the velocity of the reaction is a function of the concentration of the hydrogen ion. Esters also undergo hydrolysis and such reactions are markedly catalyzed by the hydrogen ion, or in terms of the modern Bronsted concept of acidity, by the *onium*[4] ion, or solvated proton. It was, therefore, to have been expected that the rate of ammonolysis of esters in liquid ammonia would be accelerated by the presence of ammonium salts, which have been shown to possess acid character in liquid ammonia.

It has already been demonstrated qualitatively that ammonium salts do exert a catalytic effect in other ammonolytic reactions. Blair[5] showed that urea may be converted into guanidine by heating with ammonia at 300°C., if ammonium chloride is present. Pinck[6] used a liquid ammonia solution of ammonium chloride to effect the ammonolysis of fluorenone anil to the imide and aniline. Franklin[7] pointed out that triphenylguanidine reacts with ammonia at 200°, in the presence of ammonium chloride, to give guanidine and aniline. Shatenshtein[8] demonstrated quantitatively that the ammonolysis of santonin, involving splitting of the lactone linkage, is catalyzed by various ammonium salts.

Preliminary experimental tests[9] indicated that diethylmalonate ammonolyzed to give malonamide at a sufficiently slow rate at 0° to permit of its more extended investigation. Parallel equations (3) and (4) show the effect of water and ammonia, respectively, upon diethylmalonate.

$$CH_2(COOC_2H_5)_2 + 2H_2O \rightarrow CH_2(COOH)_2 + 2C_2H_5OH \quad (3)$$

$$CH_2(COOC_2H_5) + 2NH_3 \rightarrow CH_2(CONH_2)_2 + 2C_2H_5OH \quad (4)$$

The experimental material presented in this paper deals with a study of the effect of ammonium chloride and other ammonium salts upon the rate of ammonolysis of diethylmalonate at 0° and −33°.

*Experimental.*—In studying the ammonlysis of the ester at 0° the following experimental procedure was employed: A definite weight of pure, dry ammonium salt was introduced into a dry calibrated pyrex tube (16 × 300 mm.) containing 5 cc. (5.23 g.) of diethylmalonate. The tube with its contents was cooled in a solid carbon dioxide-acetone mixture and liquid ammonia added to give a total volume of 25 cc. of solution. The tube was then sealed. Usually from ten to twenty tubes were filled and sealed at one time. The tubes were then placed in an ice bath and allowed to come to a temperature of 0°C. It was observed at the beginning of the investigation that the ester did not seem to diffuse readily into the supernatant layer of liquid ammonia. Thus the initial time of the reaction was taken as that time when the tubes had attained the temperature of the bath and were thoroughly shaken to effect complete solution. The assumption was made that there was little diffusion and reaction during the time interval between the sealing of the tube and the mixing of the contents. The tubes were allowed to stand in the thermostat for given time intervals after which they were again cooled and opened. The contents were emptied into a flask and the ammonia allowed to vaporize rapidly at atmospheric pressure. The residual ammonia was removed by applying suction. The product was thoroughly washed with ether to remove the unreacted ester and ethylmalonamate, then dried and weighed as the amide plus the ammonium salt. The weight of amide was determined by difference.

*Effect of Varying Concentrations of Ammonium Chloride on the Rate of Ammonolysis.*—Some typical results are presented in table 1 which serve to bring out clearly the effect of increasing concentration of ammonium chloride upon the yield of malonamide.

TABLE 1

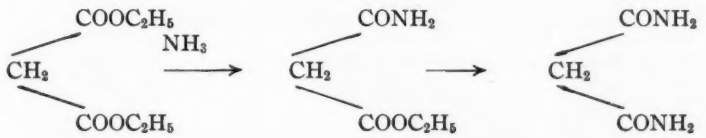
AMMONOLYSIS OF DIETHYLMALONATE—EFFECT OF VARYING AMOUNTS OF $NH_4Cl$

(14.0 ± 0.5 g. $NH_3$ plus 5.23 g. ester)

Theoretical yield of malonamide, 3.33 g.

| G. $NH_4Cl$ ADDED | YIELD OF MALONAMIDE IN GRAMS | | |
|---|---|---|---|
| | 5 HOURS | 10 HOURS | 20 HOURS |
| 0.0 | 0.09 | 0.20 | 0.30 |
| 0.2 | 0.53 | 1.00 | 2.42 |
| 0.4 | 1.02 | 1.72 | 2.83 |
| 0.6 | 1.45 | 2.38 | 2.99 |
| 0.8 | 1.96 | 2.68 | 3.00 |

It is quite evident that the yield of amide is very greatly increased by the addition of an ammonium salt, and that the yield is roughly proportional to the concentration of ammonium chloride in the early stages of the reaction. An attempt to use these and additional data for calculation of reaction velocity constants led to no conclusive numerical results, indicating that the simple overall equation given by 4 does not represent a true picture of the mechanism of the reaction. The reaction apparently proceeds in two steps, first to give ethylmalonamate as an intermediate product, which reacts further to give malonamide as the final product.




Ethylmalonamate is soluble in ether, consequently its presence in the reaction mixture led to no complications so far as determining the yield of malonamide. In our experimental procedure, the reaction product was treated with ether in order to remove both unreacted ester and half-ester.

*Effect of Equivalent Concentrations of Various Ammonium Salts.*—Shatenshtein[8] was able to show that the catalytic effect of ammonium salts on the ammonolysis of santonin varied with the acid anion in the order $ClO_4^- < I^- < NO_3^- < Br^- < Cl^-$. This order is just the reverse of what might be expected on the basis of the thermodynamic properties of these compounds. The method employed by Shatenshtein involved measurement of the change in optical rotation of the compounds under investigation and is susceptible to a high degree of accuracy. This procedure is not applicable to diethylmalonate. In the present investigation results reproducible to within ten per cent were obtained, insufficient to bring out the differences observed by the Soviet investigators. The data in table 2 indicate that equivalent concentrations of various ammonium salts are about equally effective, within the limit of experimental error of our method, in effecting the conversion of the ester to the amide.

TABLE 2

EFFECT OF EQUIVALENT CONCENTRATIONS OF VARIOUS AMMONIUM SALTS ON THE AMMONOLYSIS OF DIETHYLMALONATE

(5.23 g. Ester plus 14.0 ± 0.5 g. $NH_3$)

| Salt used | .... | $NH_4Cl$ | $NH_4Br$ | $NH_4I$ | $NH_4ClO_4$ | $NH_4C_2H_3O_2$ | $NH_3 \cdot HOOCC_4H_8$ |
|---|---|---|---|---|---|---|---|
| g. | .... | 0.20 | 0.37 | 0.54 | 0.43 | 0.29 | 0.45 |
| Yield—10 hrs. | 0.20 | 1.00 | 1.00 | 0.99 | 1.10 | 1.16 | 0.94 |
| Yield—20 hrs. | 0.30 | 2.42 | 2.58 | 2.55 | 2.34 | 2.38 | 2.45 |

*Catalytic Effect of Malonamide.*—Formally, malonamide is the nitrogen analog of malonic acid. Malonamide has been shown to possess acidic character in liquid ammonia as it reacts with potassium amide in this solvent to form a tri-potassium salt, $KHC(CONHK)_2$.[10] Since it behaves as an acid, it might also be expected to catalyze the conversion of the ester into the amide. The data in table 3 verify this assumption.

TABLE 3

CATALYTIC EFFECT OF MALONAMIDE

(5.23 g. ester plus 14.0 ± 0.5 g. $NH_3$)

| G. MALONAMIDE ADDED | YIELD OF MALONAMIDE IN GRAMS 10 HRS. | 20 HRS. |
|---|---|---|
| 0.00 | 0.20 | 0.30 |
| 0.10 | 0.24 | 1.24 |
| 0.50 | 0.26 | 1.41 |

These experiments indicate that the ammonolysis of diethylmalonate is autocatalytic in nature, since the reaction is catalyzed by one of the products of the reaction. It is highly probable that ethylmalonamate, $H_2C(CONH_2)(COOC_2H_5)$, the intermediate product, also catalyzes the reaction, since it might also be expected to behave as an acid in liquid ammonia.

*Ammonolysis of Diethylmalonate at −33°.*—In carrying out a series of experiments at −33° use was made of a liquid ammonia bath. Five cubic centimeters (5.23 g.) of diethylmalonate was placed in a tube of the same dimensions as those used in the experiments at 0°. For runs with catalyst the ammonium chloride was first introduced into the tube, after which the ester and liquid ammonia were added to give a volume of 25 cc. of solution. Typical results are given in table 4 indicating, as might have been expected, that the reaction is much slower at −33°.

TABLE 4

AMMONOLYSIS OF DIETHYLMALONATE AT −33°

| TIME IN HOURS | YIELD OF MALONAMIDE IN GRAMS USING PURE ESTER | WITH THE ADDITION OF 0.2 G. $NH_4Cl$ |
|---|---|---|
| 48 | 0.34 | 0.62 |
| 96 | 1.05 | .... |
| 120 | 1.25 | 1.68 |

[1] For a comprehensive treatise on reactions in liquid ammonia see Franklin, E. C., "Nitrogen System of Compounds," A. C. S. Monograph (1935); Reinhold Publishing Corporation, New York, N. Y.

[2] Audrieth, L. F., *Zeit. Physik. Chem.*, **165**, 323–330 (1933).

[3] Moureu H., and Wetroff, G., *Compt. rend.*, **201**, 1381–1383 (1933).

[4] Audrieth L. F., and Schmidt, M. T., *Proc. Nat. Acad. Sci.*, **20**, 221–225 (1934).

[5] Blair, T. S., *Jour. Am. Chem. Soc.*, **48**, 87–95 (1926).

[6] Pinck, L. A., and Hilbert, G. E., *Ibid.*, **56**, 490 (1934).

[7] Reference 1, page 91.

[8] Shatenshtein, A. I., *Jour. Phys. Chem.* (U. S. S. R.), **4**, 703–705 (1933); *Jour. Am. Chem. Soc.*, **59**, 432–435 (1937).

[9] Slobutsky, C., and Audrieth, L. F., *Trans. Ill. Acad. Sci.*, **29**, 104–105 (1936).

[10] Reference 1, page 276.

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## *THE STRUCTURE OF CYAMELURIC ACID, HYDROMELONIC ACID, AND RELATED SUBSTANCES*

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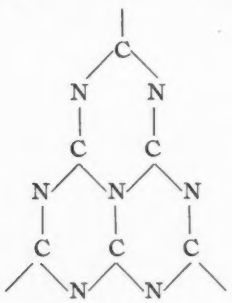
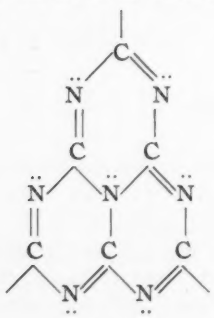
Over a century ago, in 1835, Leopold Gmelin[1] prepared the substance tripotassium hydromelonate by heating potassium ferrocyanide with sulfur; he also made other salts of hydromelonic acid, and carried out analyses, which, however, were not sufficiently accurate to lead to correct formulas. He recognized the similarity of the substances to the group of nitrogen compounds discovered and named by Justus Liebig,[2] including melon, melam, melamine, etc., and assigned names to them on this basis. Liebig[3] then prepared tripotassium hydromelonate by other methods, including, for example, the reaction of fused potassium thiocyanate with antimony trichloride, and in 1855, after much labor, he succeeded[4] in assigning to the acid essentially its correct formula, $H_3C_9N_{13}$ (using the incorrect atomic weight 6 for carbon, he wrote $C_{18}N_{13}H_3$). By decomposing hydromelonates with alkali, Henneberg[5] in 1850 prepared salts of another tribasic acid, cyameluric acid, $H_3O_3C_6N_7$, as well as the acid itself.[6] For this substance structural formulas such as $HN{=}C_3N_3{-}O{-}C_3N_3\langle^{OH}_{OH}$ and $HO{-}C_3N_3{=}N{-}C_3N_3\langle^{OH}_{OH}$, involving the cyanuric nucleus $C_3N_3$, were suggested long ago and the similar formula $N(C_3N_3{=}NH)_3$ was proposed for hydromelonic acid; formulas based on the hexamethylenetetramine nucleus have also been proposed.[7] These formulas, however, do not provide a satisfactory representation of the properties of the substances. We have been led to the belief that the substances contain a nucleus $C_6N_7$ (the "cyameluric nucleus"), which bears to the cyanuric nucleus a relation somewhat similar to that between the condensed aromatic hydrocarbons and benzene.

Four years ago Professor E. C. Franklin gave us for x-ray examination[8] a few small crystals of the substance $Na_3C_6N_9 \cdot 3H_2O$, the preliminary study of which indicated the presence of an anion $C_3N_3(NCN)_3^{=}$ similar in structure to cyanuric triazide,[9] $C_3N_3(N_3)_3$. The corresponding acid $H_3C_6N_9$ can accordingly be considered to be a derivative of cyanuric acid; it may be called either cyanuric tricyanamide, $C_3N_3(NCNH)_3$, or tricyanomelamine,[10] $C_3N_3(NHCN)_3$. The strength of the acid is to be attributed to resonance between the valence-bond structures corresponding to these representations.

This formulation of the tribasic acid $H_3C_6N_9$ suggested to us the similar formulation of hydromelonic acid as $C_6N_7(NCNH)_3$, which would thus be related to cyameluric acid, $C_6N_7(OH)_3$, as cyanuric tricyanamide is to cyanuric acid, $C_3N_3(OH)_3$. Of the possible structures for the trivalent cyameluric nucleus $C_6N_7$ which occurred to us there is one which is so reasonable and which accounts so satisfactorily for the properties of the radical that there remains little doubt as to its correctness. This structure involves a coplanar arrangement of three fused rings,



The electronic structure corresponds to resonance not only between the two valence-bond structures



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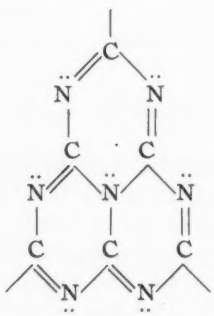
and



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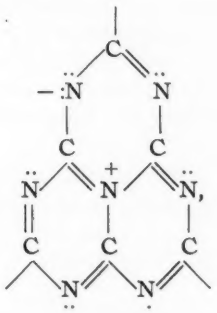
(corresponding to the Kekulé structures of benzene), but also among the eighteen structures of the type



III to XX

each of which, with six double bonds but with separated electric charges, should make a somewhat smaller contribution than structure I or II (probably about one-half or two-thirds as large). On this basis each of the six outermost C-N bonds in the nucleus would have 50% double-bond character, each of the six remaining peripheral bonds about 36% and each of the three central bonds about 28%. The corresponding values for the C-N distances predicted by use of the resonance curve and table of covalent radii,[11] with consideration also of the effect of electric charges,[12] are 1.33 Å, 1.35 Å and 1.32 Å, respectively; the $C_3N_3$ rings in the fused nucleus are thus nearly regular, and have nearly the same dimensions as expected for the cyanuric nucleus, 1.33 Å,[13] corresponding to 50% double-bond character.

The large number of important structures among which resonance can take place should make the cyameluric nucleus remarkably stable. This has been verified by a quantum mechanical calculation of the resonance energy by the molecular-orbital method, the valence-bond method in its simple form being inapplicable. Representing the C-N exchange integral by $\beta$, and assuming the greater electronegativity of nitrogen (relative to carbon) to correspond to a difference $2\beta$ in Coulomb energy,[14] we find for the cyameluric nucleus the resonance energy $7.4336\beta$, relative to structure I or II. With $\beta$ = 20,000 cal./mole (approximately the C-C value in benzene), this corresponds to stabilization by 150,000 cal./mole, or 25,000 cal./mole per double bond. (For the cyanuric nucleus a similar treatment gives $4.129\beta$ for the resonance energy, stabilizing the molecule by 27,500 cal./mole per double bond.) This large resonance energy completely removes the unsaturation expected for a non-resonating molecule with six

double bonds, and accounts for the extraordinary stability observed for cyameluric acid and hydromelonic acid and their derivatives.

Except for the changes due to the increased molecular weight, the properties of derivatives of the cyameluric nucleus should resemble those of the corresponding derivatives of the cyanuric nucleus very closely. In table 2 there are given values of the conjugation energy of various groups with both the cyanuric nucleus and the cyameluric nucleus, calculated by

TABLE 1

ENERGY VALUES CALCULATED BY THE MOLECULAR-ORBITAL METHOD

| R | ENERGY OF R[a] | $C_3N_3R_3$ | $C_6N_7R_3$ |
|---|---|---|---|
| Amino, —$NH_2$ | $4.0000\beta$ | $29.8272\beta$ | $49.2900\beta$ |
| Cyanamide, —NCNH | $9.4641\beta$ | $45.9625\beta$ | $65.3925\beta$ |
| Azide, —NNN | $10.8284\beta$ | $49.9208\beta$ | $69.3274\beta$ |
| Hydroxyl, —OH | $8.0000\beta$ | $41.1513\beta$ | $60.5323\beta$ |

Energy of $C_3N_3$ radical, $16.1290\beta$; of $C_6N_7$ radical, $35.4336\beta$.

[a] In this calculation the values $q_C = 0$, $q_N = 2\beta$ and $q_O = 4\beta$ were used for the Coulomb energies of the $p_z$ orbitals of carbon, nitrogen and oxygen, respectively.

TABLE 2

CONJUGATION ENERGIES OF GROUPS WITH THE CYANURIC AND CYAMELURIC NUCLEI

| GROUP | CONJUGATION ENERGY PER GROUP WITH CYANURIC NUCLEUS | WITH CYAMELURIC NUCLEUS | RATIO |
|---|---|---|---|
| Amino | $0.5661\beta$ | $0.6188\beta$ | 0.915 |
| Cyanamide | $0.4804\beta$ | $0.5222\beta$ | 0.920 |
| Azide | $0.4355\beta$ | $0.4695\beta$ | 0.928 |
| Hydroxyl | $0.3408\beta$ | $0.3662\beta$ | 0.931 |

subtracting the energy of the radicals $C_3N_3$ or $C_6N_7$ and 3R from that of the molecule $C_3N_3R_3$ or $C_6N_7R_3$ (table 1), and dividing by three. It is seen that these conjugation energies are closely similar for the two nuclei, the cyameluric nucleus being about 8% more effective in conjugation than the cyanuric nucleus.

We accordingly believe that a series of cyameluric derivatives analogous to the cyanuric derivatives can be prepared. Of these only a few have so far been reported. Cyameluric acid, $C_6N_7(OH)_3$, is the analog of cyanuric acid, $C_3N_3(OH)_3$; and hydromelonic acid, $C_6N_7(NCNH)_3$, is the analog of cyanuric tricyanamide, $C_3N_3(NCNH)_3$. So far as we are aware, substances which might safely be identified as the cyameluric analogs of cyanuric trichloride, $C_3N_3Cl_3$, cyanuric tricyanide, $C_3N_3(CN)_3$, melamine, $C_3N_3(NH_2)_3$, hexamethylmelamine, $C_3N_3[N(CH_3)_2]_3$, and the many other known derivatives of cyanuric acid have not been described in the literature. The preparation and study of some of these substances are being carried on in these Laboratories.

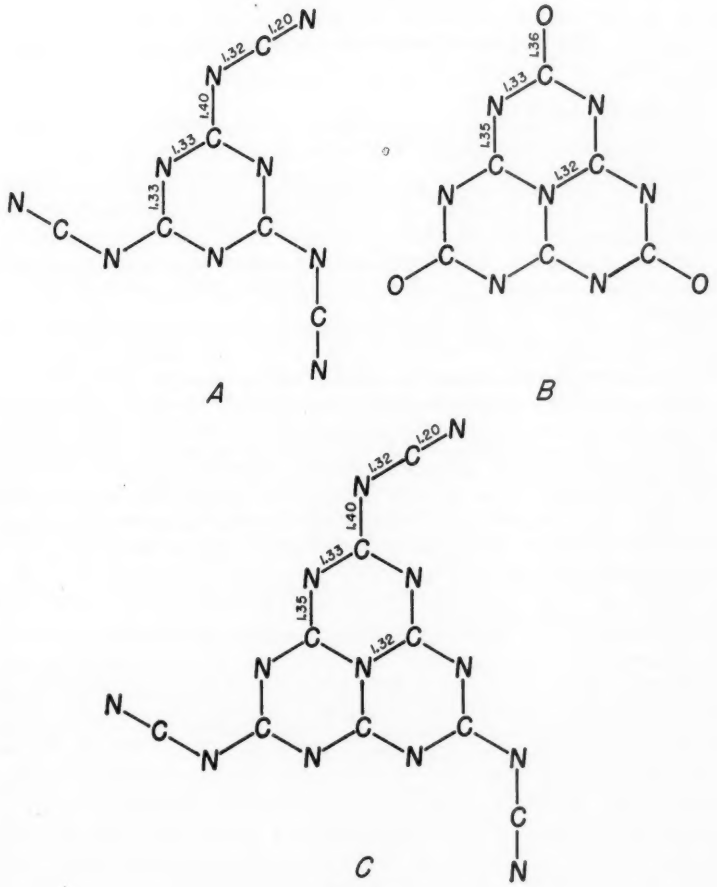



FIGURE 1

The structures of (*A*) the cyanuric tricyanamide ion, $C_6H_9^{\equiv}$, (*B*) the cyamelurate ion, $C_6N_7O_3^{\equiv}$ and (*C*) the cyameluric tricyanamide (hydromelonate) ion, $C_9N_{13}^{\equiv}$. Predicted values of interatomic distances are shown. The molecules are coplanar, with all bond angles (except in the linear cyanamide groups) close to 120°.

The configurations of the cyanuric tricyanamide ion, the cyamelurate ion and the cyameluric tricyanamide ion are shown in figure 1.

We are indebted for the gift of crystals of trisodium cyanuric tricyanamide to the late Professor E. C. Franklin. We wish to thank Dr. J. Sherman for assistance with the laborious quantum mechanical calculations.

*Contribution No. 628.

[1] L. Gmelin, *Ann. Pharmacie*, **15**, 252 (1835).

[2] J. Liebig, *Ibid.*, **10**, 1 (1834).

[3] J. Liebig, *Ann. Chem. Pharm.*, **50**, 337 (1844).

[4] J. Liebig, *Ibid.*, **95**, 257 (1855).

[5] W. Henneberg, *Ibid.*, **73**, 228 (1850).

[6] Henneberg assigned to the cyamelurates two alternative formulas, one including an extra atom of hydrogen. Analyses leading to the choice of the correct formula were later made by Liebig (Ref. 4).

[7] E. C. Franklin, "Nitrogen System of Compounds," Reinhold Publishing Corp., 1935.

[8] We learned later that crystals of the substance were also given by Professor Franklin to Dr. J. L. Hoard, who is continuing their study at Cornell University. The substance was originally identified (E. C. Franklin, *Jour. Am. Chem. Soc.*, **44**, 497 (1922)) as $NaC_3N_3 \cdot H_2O$, the sodium salt of dicyanimide. Our x-ray investigation led us to adopt the trimeric formula, which was also adopted by Professor Franklin (Ref. 4).

[9] E. W. Hughes, *Jour. Chem. Phys.*, **3**, 1 (1935); I. E. Knaggs, *Proc. Roy. Soc.*, **A150**, 576 (1935). The hexagonal unit of structure of $Na_3C_6N_9 \cdot 3H_2O$, containing two molecules, has $a_0 = 10.25$ Å and $c_0 = 6.60$ Å, whereas the corresponding dimensions for cyanuric triazide are $a_0 = 8.73$ Å, $c_0 = 5.96$ Å.

[10] Several organic tricyanomelamines have been prepared recently by J. Biechler, *Compt. Rend.*, **203**, 568 (1936).

[11] L. Pauling and L. O. Brockway, *Jour. Am. Chem. Soc.*, **59**, 1223 (1937).

[12] N. Elliott, *Ibid.*, **59**, 1380 (1937).

[13] There is evidence from electron diffraction studies of pyrazine and pyridine that this value should be increased by 0.01 or 0.02 Å because of the electronegativity of nitrogen (V. Schomaker and L. Pauling, paper to be published in *Jour. Am. Chem. Soc.*).

[14] G. W. Wheland and L. Pauling, *Ibid.*, **57**, 2086 (1935).

# SPONTANEOUS CHROMATIN REARRANGEMENTS AND THE THEORY OF THE GENE

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Spontaneous chromatin rearrangements in *Drosophila* are considered to be rare. In the few cases known they have a visible phenotypic effect comparable to so-called gene mutations whereas many of the experimentally produced rearrangements show no visible effect. The general opinion of geneticists seems to be that in such cases either a gene mutation has occurred at or near the break or that a position effect is involved. Elaborate theories have been presented to account for such a position effect on the basis of the theory of the gene (Muller, Offerman). It has not escaped notice that these position effects include many of the phenotypes of so-called gene mutations, and some geneticists have put the question whether or not all mutations are position effects. But the answer was in the negative (e.g., Muller). A series of observations, which I made during the past four years, tend to show that gene mutations do not exist and therefore no genes. Owing to enforced interruptions the analysis of my material is not yet finished, but enough is known to make a strong case.

About four years ago I found that a standard *Drosophila* stock of pure plexus had changed its phenotype into extreme plexus and partly blistered individuals. A remarkable asymmetry combined with this drew my attention, and in trying to analyze this in hundreds of lines, selections and crosses the following events occurred. One of the one-pair-broods of the plexus blistered stock yielded only a few individuals. This seemed suspicious, and another generation was bred. This consisted of typical plexus, normal and rudimentary flies, to which in the next generation a type with pointed wings and one with spread, plexus and blistered wings was added (also short bristles, which were not followed up). The former plexus blistered had disappeared simultaneously in the whole brood. It was then found that rudimentary was identical with the classic one, and that the pointed wings behaved like a recessive mutant at the left end of the *X*-chromosome. (It may be added that very rarely single rudimentary males appear in $F_2$ of crosses involving the plexus-blistered line, after the fashion of so-called gene mutations.) Obviously here a complete rearrangement had taken place in which simultaneously three "mutant" types appeared, plexus reappeared and both plexus and blistered disappeared (or wild appeared). As the whole brood was changed simultaneously, the rearrangement must have taken place in the germ tract. Following this, the plexus-blistered stock was analyzed and seemed first to contain

both plexus and blistered (or an allele of the latter). The sex ratios, however, indicated something in the *X*-chromosome, and it turned out that the echinus and rudimentary loci were involved (occasionally also white). At present—the analysis is not yet finished—it seems as if the echinus locus were inserted at the *bs*-locus of one plexus-containing chromosome, and the rudimentary locus into the other. The third chromosome is also involved, at least at the ebony locus. One of these insertions (*rud*) produces an ordinary *bs*-effect, the other an extreme *bs*-effect, both behaving like alleles. It is not yet clear which further rearrangement produces the other types, and the detailed facts are very complicated.

It is remarkable that the same line since gave other rearrangements resembling mutations. Thus a "mutation" was produced located in the *X*-chromosome and characterized by soft wings with blisters behind the cross vein; and in a few crosses between *pxbs* and the stock *bs*, the "mutant" ebony was produced, further abnormal abdomen, scute and broad wings.

While working with these rearrangements it became necessary to inquire into the stock *bs* (blistered). Among the many crosses made with this "mutant," one again (with Oregon wild) yielded a simultaneous rearrangement in all individuals of a brood: blistered disappeared, and there appeared in the following two generations plexus, dumpy vortex, thoraxate, purple and a few apparently new types, all behaving like "gene mutations" in the second chromosome but involving all members of a brood and not single individuals as had also been true in the *pxbs* case. As blistered is again involved, both cases belong together and demonstrate a large series of "gene mutations" to be produced by a series of chromatin rearrangements within the same or between different chromosomes. There are many remarkable additional details. To mention only one: We mentioned the recessive type with pointed wings at the left end of Chrom. I. A phenotypically identical type was found after heat-treatment from wild type. It turned out to be situated at the same locus. When these two "alleles" with pointed wings were crossed (both breeding perfectly true), a series of types appeared in $F_2$, $F_3$, among them *pxbs*, *px*, spread wings, soft blistered wings.

After these findings I do not doubt that all so-called gene mutations will turn out to be chromatin rearrangements. This would make the idea of position effect absurd as this effect would be now synonymous with so-called gene mutation. In other words, there are no genes, no gene mutations and no wild type allelomorphs. One may call the production of a phenotypic effect by a locus a gene, if one chooses to, and the simultaneous effects of other loci involved in the rearrangement, modifiers. But then there is no wild type allele, the whole wild type chromosome being the allele for all "mutant genes" within this chromosome. The chromosome

then is the unit, and a definite order within its texture is required for normal development. It is obvious that this will lead to a reconsideration of all such things as modifiers, specific suppressors, dominance enhancers, etc. The details of further consequences will be elaborated in another place, where we shall try also to find a chemical model for such a situation and discuss the views of others.

Why, one may ask, did all the *Drosophila* workers not hit upon such facts before? There are a number of reasons. It seems that the type of experimentation which leads to the discovery of such cases is rarely used; namely, innumerable repetitions of pair-breeding in pure stocks or in simple crosses involving "mutants" which seem to be in a rather labile equilibrium. (Besides *bs* I have reasons to assume that plexus, Beaded, balloon, vestigial, cut, black, kidney belong to this category.) Such crosses are usually made only in class work, and in this case events such as the ones described would be considered an experimental error. That, however, the same results would easily be found if looked for may be concluded from a recent paper by Plough and Holthausen[1] who report facts resembling those here reported as occurring in class work; they describe their findings as a strange case of "mass mutation." And still more characteristic, the same loci in the second chromosome, black and blistered, are involved which were also involved in my cases, in addition to extreme plexus, scute and abnormal abdomen, all of which appear also in our group of changes.

There is now a strong suspicion, almost a certainty, that the explosion of "mutations," which I observed many years ago after temperature shocks[2] in a single case and which I described as my best case of heat effect (and which never could be repeated, neither by myself nor by others), involved the same comparatively rare phenomenon. The details which I have published thus far only in a summary way parallel closely the cases here reported: The rearrangement produced simultaneously the "mutants," ebony, rolled, kidney and aristapedia. The heat treatment probably had nothing to do with the spontaneous phenomenon. Such a solution could hardly be proposed in 1929 when the theory of the gene was held an indisputable fact. The details of the case are now worthy of publication.

I do not doubt that soon others will report similar cases (even from former experience, discarded because improbable), and that the gene then will disappear completely from genetics, except for teaching purposes. A full report upon the experiments will be published later.

[1] Plough, H. H., and Holthausen, C. F., "A Case of High Mutation Frequency without Environmental Change," *Amer. Nat.*, **71** (1937).

[2] Goldschmidt, R., "Experimentelle Mutation und das Problem der sogenannten Parallelinduktion. Versuche an Drosophila." *Biol. Centrbl.*, **49** (1929).

# REGULATION OF HEAT LOSS FROM THE HUMAN BODY

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Read before the Academy October 27, 1937

The loss of heat from the body has an important rôle in the regulation of temperature but there have been surprisingly few careful measurements. Bazett and McGlone[1] and Burton[2] have made most important contributions to this subject. Winslow, Herrington and Gagge[3] who have used the Hardy radiometer, but with experimental conditions quite different from ours, have in the last few weeks published curves which are very similar to some shown in our report. The large respiration calorimeter of the Russell Sage Institute of Pathology and the radiometric apparatus recently devised by Hardy[4] make it possible to measure simultaneously all the external factors of heat production and heat loss. The technique of human calorimetry has been fully described by Lusk.[5] Precise determination of the oxygen consumption, the $CO_2$ production and the urinary nitrogen furnish the data necessary for calculation of the heat produced within the body. The water vaporized from the skin and lungs is collected and weighed, and the purely thermal loss (convection, conduction and radiation) is measured by a flow-calorimeter. The rectal temperature and the surface temperature are measured as well as the temperature of the surrounding air and walls. Measurement is also made of the relative humidity of the calorimeter. The air in the calorimeter is practically still except for the natural convection currents arising from the warm surface of the naked man.

*Experimental.*—Two normal men were chosen as subjects. Their physical data are given in table 1.

TABLE 1

| SUBJECT | AGE | HEIGHT, CM. | WEIGHT, KG. | TOTAL SURFACE AREA SQ. M. | B. M. R. (CAL. PER SQ. M. PER HR.) |
|---|---|---|---|---|---|
| D B | 54 | 179 | 77.5 | 1.95 | 34.9 |
| H | 33 | 168 | 67.0 | 1.77 | 34.8 |

They were studied nude in environments ranging from 23°C. to 35°C. under basal and other experimental conditions. Observations were made during the winter, spring and early summer months in 1935 and 1936. No seasonal changes were observed.

The day before an experiment the calorimeter thermostat is adjusted to the desired temperature. The room is provided with both heating and cooling units so that any temperature can be obtained. By 9 A. M. on the day of an experiment all necessary preparations have been completed and the calorimeter, with the cooling water circulating through the coils, has es-

tablished thermal equilibrium in all parts. The subject arrives about this time and sits in ordinary clothing for an hour in the prevailing atmosphere. As he undresses the skin temperature under the clothing is measured. Immediately after voiding he is weighed, the rectal thermometer inserted and he is then sealed in the calorimeter before 10:30 A. M. The air circulation through the calorimeter is started and the preliminary period begun. During the next half hour the subject measures his skin temperature and the radiation temperature of the calorimeter walls, top and bottom. He then

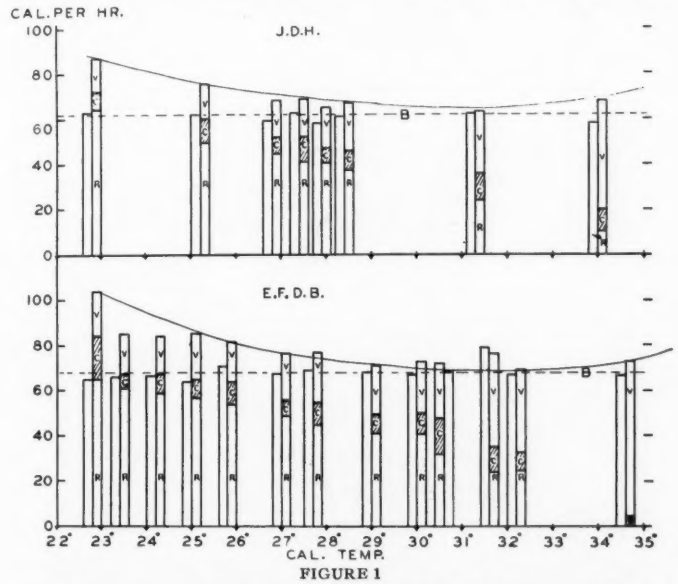


FIGURE 1

Basal experiments on two nude subjects at different calorimeter temperatures. Heat production shown in clear columns; heat loss divided into radiation, R, convection, C, and vaporization, V. Dotted line B, average basal metabolism.

remains motionless for about ten minutes and the first experimental period is started at about 11:15. During this hour the subject remains as quiet as possible. Immediately after the start of the second period the skin and wall temperatures are again measured. The second and third periods are used for studying the effects of chills, exercise or forced air currents from a fan. The surface temperature may be measured several times during these intervals. The rectal temperature is read every four minutes with a resistance thermometer so that a complete record of body temperature is obtained. The basal or control period lasts an hour unless some reaction such as an approaching chill cuts it short.

*Results.*—It was possible to obtain basal hours throughout the whole experimental range of temperatures. Periods after exercise or fan were considered basal if the heat production fell within 5 per cent of the average value for control periods, regardless of the amount of heat given off by the body. The values for the heat production, shown to the left by the clear

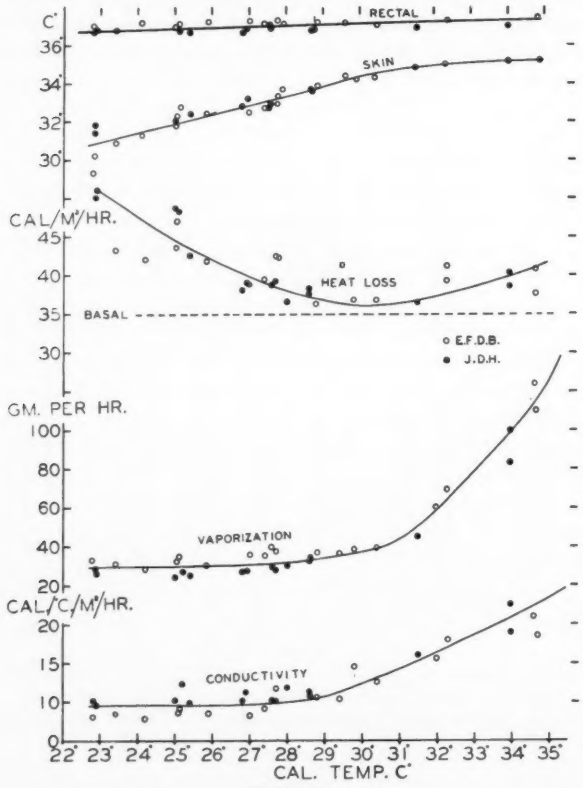


FIGURE 2

Changes in factors involved in heat loss regulation with increasing calorimeter temperatures.

columns, and the heat lost, divided into vaporization convection and radiation, are plotted for both subjects in figure 1.

Although both subjects were on the point of shivering at the end of the basal periods in many of the experiments in which the temperature was lower than 27°C., no increase in oxygen consumption was observed until the subject felt the usual waves of muscular contraction passing up from

the lower extremities. It was possible for the subjects to warn the observers of an approaching chill so that the basal period could be terminated and the chill studied in a separate period.

The effect of environment on the heat loss is evident. In the zone from 30°C. to 32°C. the body eliminated a minimal amount of heat, equal to the heat produced. This temperature range might therefore be termed the "neutral zone." The heat loss increased both in colder and warmer environments. On the cold side it increased in proportion to the fall in room

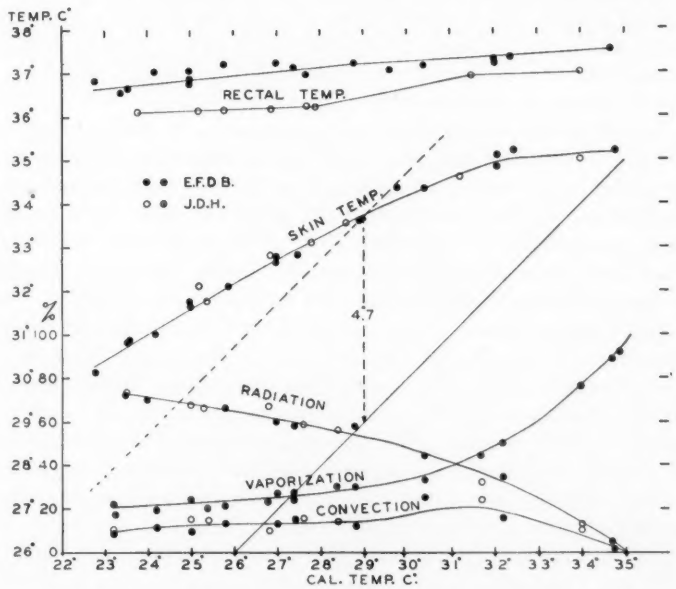


FIGURE 3

Relation of rectal temperature, skin temperature and per cent of heat loss due to radiation, vaporization and convection, to environmental temperature

temperature at the rate of approximately 3 calories per degree. This increased loss is due entirely to increased convection and radiation. Radiation, which depends only upon the difference between the skin and wall temperature, falls from 67 calories per hour and 64 calories per hour at 23°C. to zero at 35°C. Convection varies considerably from one experiment to another, and shows a definite trend only when the skin and air temperatures become nearly the same. It approaches zero at 34.7°C.

Vaporization loss is uniform up to 30°C. In environments warmer than 30°C. vaporization changes rapidly and at 34.7°C. nearly all of the body

heat is dissipated by this means. The regulation of body heat loss from 30°C. and higher temperatures is brought about by a combination of increased blood flow to the skin and by vaporization. In figure 2 are plotted the rectal and skin temperatures, heat loss, vaporization and tissue thermal conductance curves. The regulation of heat loss from the body depends upon these four factors and the surface area. The cold temperature and neutral range will be discussed separately in a subsequent paper.

In the warm air temperature zone the rectal temperature rises from an average level of 37.10 to 37.30. The surface temperature curve breaks and instead of rising 0.5°C. for every degree rise in room temperature, increases only 0.7°C. for the five degree rise from 30°C. to 35°C. It is interesting to note that although the skin temperature rises only a small amount the increase in thermal conductance of the tissues is about 75 per cent and this is due entirely to the flow of blood to the periphery. In this case increased blood flow is not accompanied by a rise in skin temperature, and as will be shown later in exercise the blood vessels of the skin may become greatly dilated while the surface temperature falls several degrees on account of the increased vaporization. The sweating of the body increases with the increased blood flow adjusting itself exactly to take care of the heat loss. The vaporization loss almost triples in the range from 30°C. to 35°C. During these warmer experiments the body is moist but no large amount of excess moisture or dripping of sweat is present. The sensitivity of the heat loss regulation in this zone is greater than in any other temperature range and seems to show an anxiety on the part of nature to prevent overheating of the body in hot weather. The parallelism between the increased blood flow and the sweating curve suggests that they are closely related phenomena. At lower temperatures when the blood flow becomes constant the vaporization curve also becomes constant.

Figure 3 shows the percentages of heat lost by radiation, conduction and convection. Radiation has a maximum value of 70 per cent in this study and decreases almost uniformly with warmer environments until it becomes zero at 35°C. Vaporization increases in importance from about 17 per cent at 23°C. to 100 per cent at 35°C. A definite bend upward in this curve occurs at about 30°C., the point of beginning sensible perspiration. Convection, the percentage value of which does not seem to change much between 23°C. and 29°C., increases from 10 per cent at 23°C. to about 15 per cent at 24°C. Between 29°C. and 32°C. convection rises to about 22 per cent, this increase probably being due to increasing velocity of the air through the calorimeter necessary to remove the water vapor. Between 32° and 35° convection decreases at a uniform rate to zero.

Vasomotor regulation of body heat loss is seen, in figure 3, to be effective down to about 28.5°C., the low temperature portion of the neutral zone. At this point the difference in skin and environmental temperature is about

5°C. If the temperature of the body is to be preserved, without increase in metabolism, this gradient should not be exceeded when the room temperature is lowered. That is, the skin temperature should fall at the same rate as the environmental temperature from this point on. This course is marked with the dashed line in figure 3. As a matter of fact the skin temperature falls at only half the rate of the environmental temperature, so that the heat lost from the body as the environment becomes cooler, must be progressively greater than that produced. This excess heat loss causes a fall in body temperature and in due time the man breaks into a chill. Figure 4 shows a series of chills brought on by exposure and also experiments with voluntary exercise. These observations were made in environments ranging from 23°C. to 30°C.

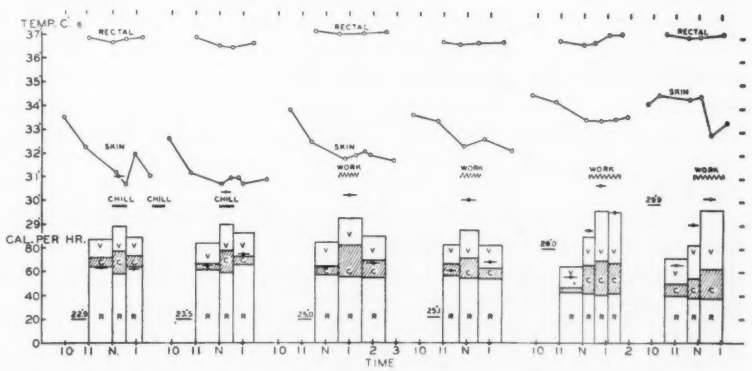


FIGURE 4

Heat production and elimination during chills and voluntary exercise. Calorimeter temperature 22.9°C. to 29.9°C. Short lines with dots represent heat production.

In the chill experiments the subject lay motionless during the preliminary period of about an hour and for another fifty to sixty minutes as a basal control period. By exerting sufficient mental effort the onset of the chill could be delayed some ten minutes and warning given to the observers in time to close the basal period. So long as the subject was not conscious of muscular tremors the oxygen consumption was not increased, and the metabolism was at the basal level, although the body was being rapidly cooled. The metabolism in the control periods of two chill experiments shown in figure 4 was 63 Calories for subject H and 65 Calories for subject D B, and the average basal levels were 62 Calories and 68 Calories, respectively. The subjects were uncomfortably cold during these periods and evidence of the "chemical regulation" of Rubner might have been expected. The fact that the metabolism remained basal practically up to the onset of the chill shows

a complete absence of such a phenomenon in these two subjects. These observations are in accord with the studies of Speck[6], Loewy[7], Johansson[8] and Benedict[9] and Swift[10], although Rubner[11], Hill[12], Martin[13] and others have found evidence of Rubner's chemical regulation.

The onset of chill was usually abrupt and after having consciously suppressed activity for a time, the subjects shook with such violence as to rock the entire calorimeter. The chill itself was usually pleasant, accompanied by a feeling of increased warmth, and it lasted generally between fifteen and twenty-five minutes. The experimental period was cut short as soon after cessation of the shivering as possible in order to find the rate of heat production. This was 100 to 150 per cent above basal while the heat eliminated increased only 10 or 15 per cent. Thus there was a considerable storage of heat in the body and the average skin temperature rose 0.5°C. to 1.5°C. The rectal temperature stopped falling and sometimes rose. With increased body temperature the men felt comfortable for perhaps an hour. The heat production fell immediately to about the basal level and the body again began to cool. As soon as the cooling was sufficient another chill resulted. Thus the only method of regulation of body temperature in these environments was repeated chills, unless voluntary exercise was used to prevent the chills.

The changes in the proportions of heat lost through the various channels deserves comment. In the basal hours radiation is maximum and convection minimum. As soon as the subject begins to move about during chill the air currents over the skin are increased with a resulting increase in convection. The radiation loss is not increased and is more often decreased, because the skin becomes cooler. Vaporization in environments below 25°C. is not appreciably affected. The increased heat loss during chill is therefore entirely due to the change in convection.

The experiments with voluntary exercise differ in no respect from those with chills. The metabolism does not happen to rise quite so high but other changes, rectal and skin temperature, convection, radiation and vaporization, all show the same tendencies as in chills. In the one experiment performed at 28°C. we find a different set of circumstances because here the subject was on the edge of vasomotor regulation. In this experiment exercise brought about a 0.4°C. rise in rectal temperature and a constant level of skin temperature. Vaporization more than doubled and convection increased about seven times; radiation remained practically unchanged. It will be noticed that the heat eliminated rose immediately upon beginning exercise to values almost double the basal heat elimination. This is in contrast to the situation during chills when the elimination changes but little. The efficiency of vasomotor regulation in preventing overheating of the body is thus contrasted to the absence of such regulation at lower temperatures.

[1] Bazett, H. C., and McGlone, B., *Arch. Neur. Psychiatry*, **27**, 1031–1069 (1932).
[2] Burton, A. C., *Jour. Nutrition*, **7**, 481–533 (1934).
[3] Winslow, C.-E. A., Herrington, L. P., and Gagge, A. P., *Am. Jour. Physiol.*, **116**, 669–684 (1936); **120**, 1–22, 133–143, 277–287, 288–299 (1937).
[4] Hardy, J. D., *Jour. Clin. Invest.*, **13**, 593–604 (1934).
[5] Lusk, G., Clin. Cal. No. 1, *Arch. Int. Med.*, **15**, 793 (1915).
[6] Speck, *Deutches Arch. Klin. Med.*, **33**, 375 (1883).
[7] Loewy, A., *Pflügers Archiv*, **44**, 189 (1890).
[8] Johansson, J. E., *Skandin. Arch. Physiol.*, **7**, 123 (1896).
[9] Benedict, F. G., *Jour. Biol. Chem.*, **20**, 263 (1915).
[10] Swift, R. W., *Jour. Nutrition*, **5**, 213 (1932).
[11] Rubner, M., *Arch. Hyg.*, **27**, 69 (1896).
[12] Hill, L., *Jour. Physiol.*, **54**, 137 (1914).
[13] Martin, C. J., *Ibid.*, **48**, 15 (1914).

## *THE PHYSICAL LAWS OF HEAT LOSS FROM THE HUMAN BODY*

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In a previous publication[1] the automatic regulation of heat loss was shown to be effective in environmental temperatures above 28°C. That is, vasomotor changes combined with activity of the sweat glands were capable of adjusting the loss of heat from the body to the heat production. In environments colder than 28°C. the body lost heat until some mechanism set off a chill and thereby increased the metabolism. With a more or less steady series of chills the temperature of the body could be maintained within the range of environments studied, down to 23°C. It was pointed out further that the thermal conductance of the body tissues remained constant below 28°C. and that no evidence of generalized vasomotor response could be found. This implies that the body reacted to temperature change in this region in much the same way as any warm inanimate object. It therefore seemed advisable to make direct comparisons between the heat loss from the human body and from a properly chosen physical object, especially as some evidence in the past would indicate that the physical laws of heat loss could not be applied directly to the human body.

*Experimental.*—An elliptical, galvanized-iron cylinder, 50 cm. long and 18 and 30 cm. in minor and major axes, was selected as having somewhat the shape of the trunk of a man and at the same time having an area which was easily calculated and completely effective in heat loss. The outer sur-

face of the cylinder was painted black with a paint whose emissivity was tested and known to be about 90 per cent. The area of the cylinder was 0.48 sq. m. and its mass when filled with water was 24.98 kg. The cylinder and its contents were heated by means of a small direct current motor which ran submerged and at the same time furnished the stirring for the water. The caloric input was measured with a carefully calibrated voltmeter and ammeter. The temperature of the cylinder was determined to 0.01°C. with a precision resistance thermometer, and the surface temperature was measured with a radiometer. The thermal capacity of the cylinder was calculated from approximations of the known masses of different materials used in its construction to be 20.9 kg. cal. per degree. The constant was also determined experimentally from data on cooling and heating. The result of 20 measurements resulted in the value 20.69 ± 0.22. The cylinder was mounted on four insulating posts, four inches from the floor of the large respiration calorimeter of the Russell Sage Institute of Pathology. In this way the factor of heat loss through conduction was eliminated and Newton's law of cooling in still air could be applied to the heat lost from the surface of the cylinder. The factor of thermal conduction was eliminated from the studies on human subjects by having the subject suspended in a tight hammock of coarse fish line with a 4-cm. mesh. Newton's law of cooling is:

$$Q = k(T_1 - T_c) \times t$$

Where, $Q$ = the heat lost
$k$ = a constant
$T_1$ = the internal temperature
$T_c$ = the calorimeter temperature
$t$ = time

An example of the applicability of this formula is given in table 1.

TABLE 1

| PERIOD | ELECTRICAL INPUT, CALS. | CALORIMETER HEAT, CALS. | DIFFERENCE, PER CENT | NEWTON'S LAW CONSTANT |
|---|---|---|---|---|
| 1 | 13.48 | 13.32 | −1.2 | 1.64 |
| 2 | 13.53 | 13.69 | +1.2 | 1.63 |
| 3 | 14.68 | 14.54 | −1.0 | 1.63 |
| 4 | 14.98 | 14.57 | −2.7 | 1.65 |

It is seen that Newton's law applies to the cylinder with an accuracy better than the agreement between the electric calorimeter and the respiration calorimeter. The disparity between the calorimeters was always less than 5 per cent and in general was not greater than 2.5 per cent. The values of the heat loss determined from the electrical input were usually in better agreement within themselves than those from the respiration calorimeter.

The heat loss from the cylinder was determined with the ventilation pump of the calorimeter running at the usual rate and with the pump shut off. The values of the Newton's law constant were not changed appreciably. Raising the cylinder from its usual position 10 cm. from the floor to a position 30 cm. from the floor caused the constant to change from 1.64 to 1.72. This change was undoubtedly due to the increased convection loss in the elevated position. The position of the human subjects was more nearly 5 cm. to 10 cm. from the calorimeter floor, and the position of the cylinder at 10 cm. was used as standard.

*Discussion.*—In order to make a comparison between the heat lost from the subjects with that from the cylinder, the vaporization loss from the skin and lungs must be omitted. That is, only the heat that is actually absorbed by the calorimeter is considered. Experiments at calorimeter temperatures between 25°C. and 26°C., show that between 66 per cent and 68 per cent of the total heat lost from the subjects was radiation, 13 per cent to 15 per cent was convection and about 21 per cent vaporization. Therefore, of the purely thermal loss from the men, 80 per cent was radiation and 20 per cent convection. The values for radiation and convection from the cylinder were 73 per cent and 27 per cent. If the radiation loss of the cylinder be increased by about 10 per cent to correct for the lower emissivity of the black paint, the proportions become 79 per cent and 21 per cent for radiation and convection. Thus on a comparable basis the proportions of heat lost through radiation and convection from the humans was the same as that from the cylinder.

In the environmental temperature range from 28°C. to 23°C. twenty experimental periods were obtained on the two subjects which may be studied in relation to Newton's cooling law and which may be compared directly with the experiments on the cylinder. These experiments were basal hours during which the nude subjects lay practically motionless for the entire time. The experimental routine for these experiments has been described. Ten experiments were performed on each subject and Newton's law applied to the data to obtain the cooling constant. This formula is:

$$C = H/(T_s - T_c) \times t \times A$$

Where $C$ = cals. per degree per hour per sq. m.
$H$ = heat measured by the calorimeter
$t$ = time in hours
$A$ = total surface area (DuBois)
$T_s$ = skin temperature
$T_c$ = calorimeter temperature

All values of $C$ lay between 4.8 and 5.8 for both subjects and averaged 5.2 cals. per degree per sq. m. Converting the data from the cylinder into the

same units, $C$, for the cylinder, comes out 6.75. It might seem surprising that the cylinder which radiated more poorly than the men should have a greater cooling constant, but it must be kept in mind that some of the area of the human body is not effective in losing heat. This difference in the cooling constants then provides an opportunity for determining the effective heat loss area of the human subject, a most important factor which is extremely difficult to measure. Simple proportion shows that after correcting for the lower emissivity of the black paint, 77 per cent of the total surface area, when the body is lying stretched out hands close to the body, is effective in heat loss. Photographic methods have given the result of 80 per cent, and wrapping the subjects in paper "mummy fashion" yields the result of 78 per cent. Other values from different laboratories have ranged from 75 per cent to 85 per cent. We have selected the value of 78 per cent for our standard body position, the military position, as being the effective radiating area.

Other experiments were performed on the same subjects in which exercise and forced air currents were studied. It was found immediately that the value of $C$ was no longer constant. Heat loss increased with a fall in skin temperature, and the heat loss was no longer proportional to the difference between skin and air temperatures. This phenomenon is to be expected from the large increases in convection produced by the fan and by the bodily movements of the subjects. Newton's simple law which applies only to still air would not be expected to be valid in these cases, and a more general form, to take into account the movements of the air over the body surface, would have to be devised. It should be possible to empirically standardize certain body movements in terms of linear air velocity.

Barr and DuBois[2] after studying heat loss in malarial chill pointed out that Newton's law of cooling could not be strictly applied to such cases, as more heat could be lost through a cold skin than through a warm skin. It has been found that in nearly all cases in which the body is losing large quantities of heat the skin cools. The factors of heat loss which depend largely upon temperature difference usually play the smaller rôle in eliminating heat from the exercising body, and the lower skin temperature is much more important to the internal gradients, as suggested by Barr and DuBois, than to the external gradients.

In figure 1 has been plotted the curve for the heat loss by convection and radiation against calorimeter temperature. The curves for the rectal and skin temperature have also been included together with the thermal conductance of the peripheral tissue. The transfer of heat from the internal organs of the body through the skin into the environment may be expressed in the usual way[3,4] by two equations.

$$\text{I.} \qquad K = \frac{H}{A(T_R - T_S)} \qquad \text{and}$$

$$\text{II.} \qquad C = \frac{H}{A(T_S - T_c)}$$

$K$ = thermal conductance of tissue
$H$ = heat lost
$A$ = total area of body
$T_R$ = rectal temperature
$T_S$ = skin temperature
$T_c$ = calorimeter temperature

Equation I has to do with the internal thermal conductance of the body tissue and equation II with the already discussed Newton's cooling law. Equation II represents the thermal transfer of heat from the skin into the environment and $C$ is constant over the range of temperatures from 22°C. to 30°C. At this point visible sweating begins and the body cooling no longer depends to any great extent upon $T_S - T_c$.

The value $K$ represents the thermal conductivity of the peripheral tissue, and in C. G. S. units has the value of

$$K = 0.00024 \text{ gm. cal./degree/cm.}^2\text{/sec.}$$

Measurements of thermal gradients in man indicate that a depth of 2 to 3 cm. is involved in the thermal gradient from the internal tissue to the skin surface. Assuming an average depth of 2 cm. for the whole body

$$K^1 = 0.00048 \text{ gm./degree/cm.}^2\text{/sec./cm.}$$

Lefèvre[5] in 1911 arrived at the value 0.00066. Comparing this value with other substances shows that aside from substances which have considerable air space, such as wool, hair felt, etc., few materials have higher insulating ability than living tissue. Leather, for example, has a value 0.0004, paper 0.0003 and cork 0.0007. It would thus appear that living tissue could hardly increase its thermal insulating ability if it had no circulation of blood, and that the heat transferred through the tissue in this environmental range is due to pure conduction. This would account for the constant value of the tissue conductance from 28°C. down. The body in this region may be compared to a cylinder of the same area as a man, wrapped with a layer of paper 1 cm. thick, the internal temperature of which is kept at 37°C. Then upon exposure to different environments the heat loss and surface temperature of the cylinder can be computed. In figure 1 the open circles represent such a computation, and the lines represent the average data from the human subject. The agreement is well within the experimental error from 28°C. to 23°C. From the foregoing it would appear that superficial circulation plays little or no rôle in heat transfer in this region. This would account for the fact that vasoconstriction, as a significant fac-

tor, is finished after 28°C. and the body cools without physiological restraint until onset of chill.

That peripheral blood flow is very small may easily be seen, for if the

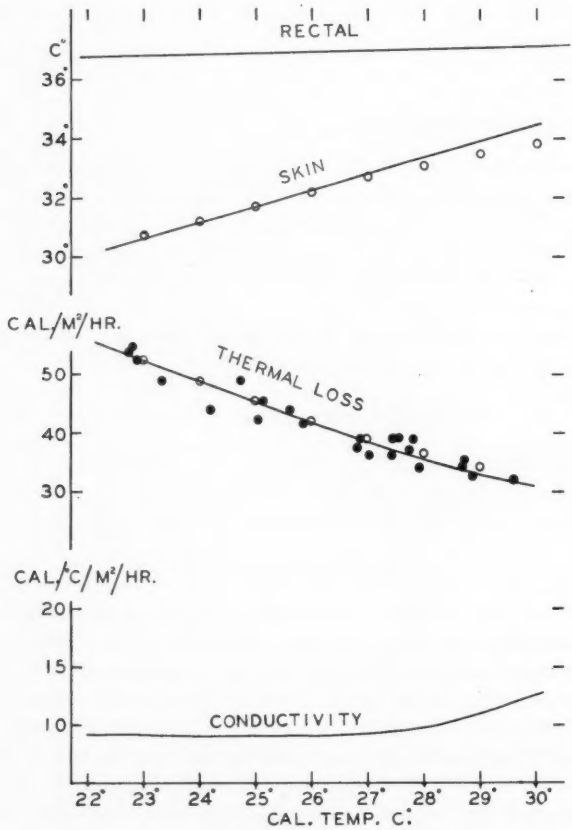


FIGURE 1

Relationship between thermal properties of the body and an inanimate object and calorimeter temperature. Solid lines represent average values from measurement on two subjects. Solid dots, observed values of thermal loss on two subjects. Open circles, calculated values from cooling law.

tissue were impermeable to heat and all the body heat transferred to the surface by the blood stream, the flow would be only about a drop every ten minutes for each sq. cm. of body surface. As the flow must be smaller than

this, the circulating blood may be considered to play a minor rôle in superficial heat transfer in this temperature zone.

Between 28°C. and 30°C., the thermal conductance begins to increase and the superficial blood flow may thus be considered to increase.

In conditions of rest or light activity there is no visible sweating in this zone. The heat eliminated from the body is approximately equal to the heat production without either shivering or sweating. This zone might therefore be termed the zone of pure vasomotor regulation. The skin temperature corresponding to this environmental temperature is about 33.8°C. and measurements made under the clothing of our subjects at the start of the experiments showed a constant skin temperature of 33.8°C. in environments from 25°C. to 32°C. Thus indoor clothing stretches the neutral zone from 2 to 7 degrees, and with the addition of heavier clothing the lower temperature limit may be extended almost indefinitely.

[1] Hardy, J. D., and DuBois, E. F., *Proc. Nat. Acad. Sciences*, **23**, 624–631 (1937).
[2] Barr, D. P., and DuBois, E. F., *Arch. Int. Med.*, **21**, 627 (1918).
[3] Winslow, Herrington, and Gagge, *Amer. Jour. Physiol.*, **116**, 669 (1936).
[4] Burton, A. C., *Jour. Nutrition*, **7**, 497 (1934).
[5] Lefèvre, J., *Chaleur Animale*, Section III, 398 (1911).

# *INDEX*


ABELSON, P. See Cook, S. F., 528.
Absorption of radio-sodium (Hamilton), 521.
ADELSON, D. E., AND BOGERT, M. T. The Synthesis of Gamma-Methyl-5,6-Cyclopentenoretene, a Compound Structurally Related to "Diels' Hydrocarbon," 117.
AEBERSOLD, P. C. See Snell, G. D., 374.
Algebra (Brauer and Nesbitt), 236.
Algebraic functions (Zariski), 410.
Algebraic theory (v. Neumann), 16.
Algebras (Jacobson), 240.
Ammonia, liquid (Slobutsky, Audrieth and Campbell), 611.
Antagonism of neurohumors (Parker), 596.
Antidromic responses (Parker), 595.
Approximation by polynomials (Sewell), 491.
Arithmetics of rings (v. Neumann), 341.
Arithmetic theory (Zariski), 410.
Atomic nuclei (Harkins), 120.
ATWOOD, S. The Last Premeiotic Mitosis and Its Relation to Meiosis in Gaillardia, 1.
AUDRIETH, L. F. See Slobutsky, C., 611.
Autosomal lethal mutation frequencies (Plough and Child), 435.
Auxin (Yin), 174; (van Overbeek), 272.
AXTMAN, G. See Bonner, J., 453.

BABCOCK, H. D. Internuclear Distance in Oxygen Molecules, 301.
Barriers, potential (Muskat and Hutchisson), 197.
BARTLEY, M. A. See Robbins, W. J., 385, 388.
Barstow miocene, California (Stock), 398.
BEADLE, G. W. Development of Eye Colors in Drosophila: Fat Bodies and Malpighian Tubes as Sources of Diffusible Substances, 146.
BEADLE, G. W., AND EPHRUSSI, B. Ovary Transplants in Drosophila Melanogaster: Meiosis and Crossing-Over in Superfemales, 356.
BEADLE, G. W. See Thimann, K. V., 143.
BEAL, J. M. Bud Development in Lilium Harrisii Following Treatment with Indoleacetic Acid, 304.
Beams, theory of (Reissner), 328.
Benzene-nitrobenzene interface (Gortner and Bull), 256.
Bernoulli numbers (Vandiver), 555.
BERRY, E. W. Succession of Fossil Floras in Patagonia, 537.
Binary quadratic discriminants (Hall), 414.
BIRKHOFF, G. On the Integration of Operators, 11.
BLESS, A. A. Effects of the Length of X-Ray Waves on Seeds, 194.
Blood (Scott and Cook), 265.
BONNER, J., AND AXTMAN, G. The Growth of Plant Embryos in Vitro. Preliminary Experiments on the Rôle of Accessory Substances, 453.
BOGERT, M. T. See Adelson, D. E., 117.
BRAUER, R., AND NESBITT, C. On the Regular Representations of Algebras, 236.
BRIDGMAN, P. W. Polymorphic Transitions of Inorganic Compounds to 50,000 kg./cm.$^2$, 202.
BUCK, J. B. Growth and Development of the Salivary Gland Chromosomes in Sciara, 423.
Bud development (Beal), 304.
BULL, H. B. See Gortner, R. A., 256.

Calculus of variations (Menger), 244.
California Eocene (Stock), 48.
California, Miocene (Stock), 398.
CAMPBELL, L. See Sterne, T. E., 115.
CAMPBELL, R. W. See Slobutsky, C., 611.
Carotenoids (Fox), 295.
CASTLE, W. E. See King, H. D., 56.
Catalysis, acid (Slobutsky, Audrieth and Campbell), 611.
Catfish Ameiurus (Parker), 595.
CHANDRASEKHAR, S. The Stability of the Radiative Gradients in the Interior of a Star, 572.
Character (Sinnott), 224.
CHEVAIS, S. See Ephrussi, B., 428.
Chicks (Scott and Cook), 265; (Cook, Scott and Abelson), 528.
CHILD, G. P. See Plough, H. H., 435.
Chlorella vulgaris (Yin), 174.
CLOUDMAN, A. M. See Little, C. C., 535.
Chromatin rearrangements (Goldschmidt), 621.
Chromosomal deficiencies (Poulson), 133; (Metz), 137.
Chromosomes (Steinberg), 54; (Marshak), 362.
Chromosomes, induced breaks in (Kaufmann and Demerec), 484.
Chromosomes, salivary (Buck), 423.
Chromosome X (Tan), 351.
Chromosome Y (Sturtevant), 360.
CLIFFORD, A. H. Representations Induced in an Invariant Subgroup, 89.
Cluster of nebulae (Zwicky), 251.
Coleoptile (van Overbeek), 272.
Color changes (Parker), 206.
Complex (Whitney), 285.
CONDON, E. U. Immersion of the Fourier Transform in a Continuous Group of Functional Transformations, 158.
Conformal geometry (Kasner), 337.
Conglomerate, Poway (Stock), 48.
Continuous rings (v. Neumann), 341.
COOK, S. F., SCOTT, K. G., AND ABELSON, P. The Deposition of Radio Phos-

phorus in Tissues of Growing Chicks, 528.
COOK, S. F. See Scott, K. G., 265.
COONFIELD, B. R. The Regeneration of Plate Rows in Mnemiopsis Leidyi, Agassiz, 152.
COOPER, K. W. Reproductive Behavior and Haploid Parthenogenesis in the Grass Mite, Pediculopsis Graminum (Reut.) (Acarina, Tarsonemidae), 41.
Copper, magnetic effects in (Hall), 600.
Corallines, genera of (Manza), 44, 561, 568.
Corpuscles (Zwicky), 106.
Co-sets (Vandiver), 552.
Crossing-over (Steinberg), 54.
Crossing-over in superfemales (Beadle and Ephrussi), 356.
CROZIER, W. J. Strength - Duration Curves and the Theory of Electrical Excitation, 71.
CROZIER, W. J., AND HOLWAY, A. H. On the Law for Minimal Discrimination of Intensities. I, 23.
CROZIER, W. J., WOLF, E., AND ZERRAHN-WOLF, G. Specific Constants for Visual Excitation, 516.
CROZIER, W. J. See Holway, A. H., 509.
Crustaceans (Welsh), 458.
Culture, tissue (Tukey), 577.
Cyameluric acid (Pauling and Sturdivant), 615.

Deficiencies, chromosomal (Poulson), 133; (Metz), 137.
DEMEREC, M. See Fricke, H., 320; see Kaufmann, B. P., 484.
Development of buds (Beal), 304.
"Diels' hydrocarbon" (Adelson and Bogert), 117.
Diethylmalonate, ammonolysis of (Slobutsky, Audrieth and Campbell), 611.
Differential geometry (Michal) 546; (Michal and Hyers), 590.
Diffusible substances (Ephrussi and Chevais), 428.
Diffusion, equation of (Epstein), 94.
Discriminants, binary quadratic (Hall), 414.
Discrimination of intensities (Crozier and Holway), 23; (Holway and Crozier), 509.
Dissociation of marine eggs (Tyler and Horowitz), 369.
Distribution of gene frequencies (Wright), 307.
Dominant spotting mutation (Little and Cloudman), 535.
DOUDOROFF, P. See Sumner, F. B., 211.
DOWKER, C. H. Hopf's Theorem for Non-Compact Spaces, 293.
Drosophila (Thimann and Beadle), 143; (Beadle), 146; (MacKnight), 440.
Drosophila eye colors (Ephrussi and Chevais), 428.
Drosophila Melanogaster (Steinberg), 54; (Poulson), 133; (Beadle and Ephrussi), 356; (Hadorn), 478; (Kaufmann and Demerec), 484.
Drosophila, mutation in (Plough and Child), 435.
Drosophila Pseudoöbscura (Tan), 351; (Sturtevant), 360.
DUBOIS, E. F. See Hardy, J. B., 624.
DUNN, L. C. A Third Lethal in the *T* (Brachy) Series in the House Mouse, 474.

Eggs, marine (Tyler and Horowitz), 369.
Electric moment of $Al_2O_3$ (Gortner and Bull), 256.
Electrical excitation (Crozier), 71.
Electrokinetics (Gortner and Bull), 256.
Embryonic development of Drosophila Melanogaster (Poulson), 133.
Embryos (Willier, Rawles and Hadorn), 542.
Embryos, plant (Bonner and Axtman), 453.
Eocene (Stock), 48.
EPHRUSSI, B., AND CHEVAIS, S. Development of Eye Colors in Drosophila: Relation between Pigmentation and Release of the Diffusible Substances, 428.
EPHRUSSI, B. See Beadle, G. W., 356.
EPSTEIN, P. S. On the Equation of Diffusion, 94.
——. On the Magnetic Energy of Supraconductors, 604.
Erythrophores in Squirrel fish (Parker), 206.
Euler numbers (Vandiver), 555.
Evolutionary analysis of species (Kinsey), 5.
Excitation, visual (Crozier, Wolf and Zerrahn-Wolf), 516.
Eye colors (Thimann and Beadle), 143; (Beadle), 146; (Ephrussi and Chevais), 428.

Fat bodies (Beadle), 146.
Films, Langmuir-Blodgett (Germer and Storks), 390.
Fish, squirrel (Parker), 206.
Foundation, yielding (Reissner), 328.
Fourier transform (Condon), 158.
Fowl (Willier, Rawles and Hadorn), 542.
FOX, D. L. Carotenoids and Other Lipoid-Soluble Pigments in the Sea and in Deep Marine Mud, 295.
FOX, D. L. See Young, R. T., 461.
FRED, E. B. See Wilson, P. W., 503.
FRICKE, H., AND DEMEREC, M. The Influence of Wave-Length on Genetic Effects of X-Rays, 320.
Fruits, deciduous (Tukey), 577.
Function, Green's (Walsh), 84, 166.
Function, partition (Rademacher), 78.
Functional equations (Hyers), 496.

Functions (Zariski), 410.
Fossil floras (Berry), 537.

Gaillardia (Atwood), 1.
Galactic structure (Miller), 405.
Galaxies (Shapley), 449.
Gamma-Methyl-5,6-Cycolpentenoretene (Adelson and Bogert), 117.
GARDNER, N. L. See Setchell, W. A., 169.
Gene frequencies (Wright), 307.
Gene structure (Metz), 137.
Gene, theory of (Goldschmidt), 621.
Genera of corallines (Manza), 44, 561, 568.
Generators (Miller), 234, 280, 333, 446, 494.
Genes (Sinnott), 224.
Genetic effects of X-rays (Fricke and Demerec), 320.
Geometries, continuous (v. Neumann), 16.
Geometry (Michal), 546.
Geometry, conformal (Kasner), 337.
Geometry, general differential (Michal and Hyers), 590.
GERMER, L. H., AND STORKS, K. H. The Structure of Langmuir-Blodgett Films of Stearic Acid, 390.
Gland, salivary (Buck), 423.
GLEYZAL, A. Linear Orders, 291; Transfinite Real Numbers, 581.
Goby (Young and Fox), 461.
GOLDSCHMIDT, R. A Remarkable Parallelism, 219.
——. Spontaneous Chromatin Rearrangements and the Theory of the Gene, 621.
GORTNER, R. A., AND BULL, H. B. Electrokinetics. XIX. Interfacial Energy and the Molecular Structure of Organic Compounds. V. The Electric Moment of $Al_2O_3$:Benzene-Nitrobenzene Interface, 256.
Grass mite (Cooper), 41.
Green's function (Walsh), 84, 166.
GREENSTEIN, J. L. See Whipple, F. L., 177.
Group, continuous (Condon), 158.
Group, symmetric (Murnaghan), 277, 488.
Groups (Miller), 13, 234, 280, 333, 446, 494, 549, 587.
Growing chicks (Cook, Scott and Abelson), 528.
Growth in roots (Robbins and Bartley), 385.
Growth of phycomyces (Robbins and Kavanagh), 499.
Growth of plant embryos in vitro (Bonner and Axtman), 453.

HADORN, E. An Accelerating Effect of Normal "Ring-Glands" on Puparium-Formation in Lethal Larvae of Drosophila Melanogaster, 478.
HADORN, E. See Willier, B. H., 542.
HALL, E. H. The Four Transverse Magnetic Effects in Copper: New Measurements, 600.
HALL, N. A. Binary Quadratic Discriminants with a Single Class of Reduced Forms in Each Genus, 414.
HAMILTON, J. G. The Rates of Absorption of Radio-Sodium in Normal Human Subjects, 521.
Hamiltonian subgroup (Miller), 587.
Haploid ovarian tissue (MacKnight), 440.
HARDY, J. D. The Physical Laws of Heat Loss from the Human Body, 631.
HARDY, J. D., AND DUBOIS, E. F. Regulation of Heat Loss from the Human Body, 624.
HARKINS, W. D. The Intermediate Nucleus in the Disintegrative Synthesis of Atomic Nuclei: Disintegration in Steps, 120.
Hearing, psychophysics of (Upton and Holway), 29, 32.
Heart beat, rate of (Welsh), 458.
Heat loss from human body (Hardy and DuBois), 624; (Hardy), 631.
HECHT, S. The Instantaneous Visual Threshold after Light Adaptation, 227.
HOFFLEIT, D. Spectroscopic Absolute Magnitudes of Three Hundred and Seventy Southern Stars, 111.
HOGAN, A. G. See Robbins, W. J., 388.
HOLWAY, A. H., AND CROZIER, W. J. On the Law for Minimal Discrimination of Intensities. II, 509.
HOLWAY, A. H. See Crozier, W. J., 23; see Upton, M., 29, 32.
Hopf's theorem (Dowker), 293.
Hormone, eye-stalk (Welsh), 458.
HOROWITZ, N. H. See Tyler, A., 369.
House mouse (Dunn), 474; (Little and Cloudman), 535.
Human body, heat loss (Hardy and DuBois), 624; (Hardy), 631.
HUTCHISSON, E. See Muskat, M., 197.
Hybrids, interracial (Sturtevant), 360.
Hydromelonic acid (Pauling and Sturdivant), 615.
HYERS, D. H. On Functional Equations in Linear Topological Spaces, 496.
HYERS, D. H. See Michal, A. D., 590.

Indoleacetic acid (Beal), 304.
Induction, stimulative and inhibitive (Witschi), 35.
Inheritance of sex (Kimball), 469.
Inheritance, quantitative (Sinnott), 224.
Inorganic compounds (Bridgman), 202.
Integration of operators (Birkhoff), 11.
Intensities, discrimination of (Crozier and Holway), 23.
Intensities, minimal discrimination of (Holway and Crozier), 509.
Interaction, vibration-rotation (Rosenthal and Motz), 259.
Interfacial energy (Gortner and Bull), 256.

Interior of stars (Chandrasekhar), 572.
Internuclear distance (Babcock), 301.
Interstellar radio disturbances (Whipple and Greenstein), 177.
Invariants, differential (Michal and Hyers), 590.
Invariant subgroup (Walsh), 89.
Ionization theory (Nurnberger), 189.
Iridophycus (Setchell and Gardner), 169.
Irradiation with neutrons (Snell and Aebersold), 374.

JACOBSON, N. Simple Lie Algebras of Type A, 240.

VON KÁRMÁN, T. On the Statistical Theory of Turbulence, 98.
KAUFMANN, B. P., AND DEMEREC, M. Frequency of Induced Breaks in Chromosomes of Drosophila Melanogaster, 484.
KAVANAGH, F. See Robbins, W. J., 499.
KASNER, E. Trihornometry: A New Chapter of Conformal Geometry, 337.
Keplerian systems (Pasternack), 91.
KIMBALL, R. F. The Inheritance of Sex at Endomixis in Paramecium, 469.
KING, H. D., AND CASTLE, W. E. Linkage Studies of the Rat (Rattus Norvegicus). II, 56.
KINSEY, A. C. An Evolutionary Analysis of Insular and Continental Species, 5.

Langmuir-Blodgett Films (Germer and Storks), 390.
LARSEN, M. J. See Lewis, D., 415.
Larvae, lethal (Hadorn), 478.
Lattices (Wallman), 164.
LAUGHLIN, H. H. The Coefficient of Prediction-Accuracy, 60.
Lethal in Mouse (Dunn), 474.
Level curves (Walsh), 84, 166.
LEWIS, D., AND LARSEN, M. J. The Cancellation, Reinforcement and Measurement of Subjective Tones, 415.
Lie algebras, simple (Jacobson), 240.
Light (Zwicky), 106.
Light adaptation (Hecht), 227.
Lilium Harrisii (Beal), 304.
Linear orders (Gleyzal), 291.
Linkage in the rat (King and Castle), 56.
Lipoid-soluble pigments (Fox), 295.
LITTLE, C. C., AND CLOUDMAN, A. M. The Occurrence of a Dominant Spotting Mutation in the House Mouse, 535.

MACKNIGHT, R. H. Haploid Ovarian Tissue in Drosophila, 440.
Magnetic effects in copper (Hall), 600.
Magnetic energy of supraconductors (Epstein), 604.
Magnitudes, spectroscopic absolute (Hoffleit), 111.
Malpighian tubes (Beadle), 146.
MANZA, A. V. The Genera of the Articulated Corallines, 44.
——. Some North Pacific Species of Articulated Corallines, 561.
——. New Species of Articulated Corallines from South Africa, 568.
Marine eggs (Tyler and Horowitz), 369.
Marine mud (Fox), 295.
MARSHAK, A. The Effect of X-Rays on Chromosomes in Mitosis, 362.
Mean value of $r^s$ (Pasternack), 91.
Meiosis in Gaillardia (Atwood), 1.
Meiosis in superfemales (Beadle and Ephrussi), 356.
Melanin in fishes (Sumner and Doudoroff), 211.
Melanophore nerves (Parker), 595.
MENGER, K. Metric Methods in Calculus of Variations, 244.
Metric methods (Menger), 244.
METZ, C. W. Deficiencies and Structural Variations within the Giant Chromosomes in Relation to the Problem of Gene Structure, 137.
Mice, male (Snell and Aebersold), 374.
MICHAL, A. D. General Projective Differential Geometry, 546.
MICHAL, A. D., AND HYERS, D. H. Differential Invariants in a General Differential Geometry, 590.
Milky Way (Miller), 405.
MILLER, F. D. Note on Galactic Structure: The Milky Way from Aquila to Cygnus, 405.
MILLER, G. A. Groups Which Contain an Abelian Subgroup of Prime Index, 13.
——. The Groups of Order $p^m$ Which Have $m - 1$ Independent Generators, 234.
——. Groups of Order Less Than $2^m$ Having $m - 1$ or $m - 2$ Independent Generators, 280.
——. Groups Having a Maximum Number of Independent Generators, 333.
——. Groups in Which Every Set of Independent Generators Is a Maximum Set, 446.
——. Sets of Independent Generators of a Finite Group, 494.
——. Groups in Which Every Subgroup of Composite Order is Invariant, 549.
——. Groups Which Contain a Hamiltonian Subgroup of Odd Prime Index, 587.
Mite, grass (Cooper), 41.
Mitosis (Marshak), 362.
Mitosis, last premeiotic (Atwood), 1.
Mnemiopsis Leidyi, Agassiz (Coonfield), 152.
Molecular structure (Gortner and Bull), 256.

Molecules, oxygen (Babcock), 301.
MOTZ, L. See Rosenthal, J. E., 259.
Mouse, house (Dunn), 474; (Little and Cloudman), 535.
Mud, marine (Fox), 295.
MURNAGHAN, F. D. The Irreducible Representations of the Symmetric Group, 277.
MURNAGHAN, F. D. On the Direct Product of Irreducible Representations of the Symmetric Group, 488.
MUSKAT, M., AND HUTCHISSON, E. Symmetry of the Transmission Coefficients for the Passage of Particles through Potential Barriers, 197.
Mustelus, pectoral bands of (Parker), 596.
Mutation frequencies (Plough and Child), 435.

Nebulae (Zwicky), 251.
Nerves, melanophore (Parker), 595.
NESBITT, C. See Brauer, R., 236.
v. NEUMANN, J. Algebraic Theory of Continuous Geometries, 16.
——. Continuous Rings and Their Arithmetics, 341.
——. Erratum, 593.
Neurohumors, antagonism in (Parker), 596.
Neutrons (Snell and Aebersold), 374.
Nitrogen fixation (Wilson and Fred), 503.
Non-compact spaces (Dowker), 293.
North Pacific, Corallines (Manza), 561.
Nuclei, atomic (Harkins), 120.
Numbers, transfinite real (Gleyzal), 581.
NURNBERGER, C. E. Ionization Theory and Radio-Biological Reactions, 189.

Operators, integration of (Birkhoff), 11.
Orders, linear (Gleyzal), 291.
Ovary transplants (Beadle and Ephrussi), 356.
VAN OVERBEEK, J. Effect of the Roots on the Production of Auxin by the Coleoptile, 272.
OXTOBY, J. C. Note on Transitive Transformations, 443.
Oxygen molecules (Babcock), 301.

$pO_2$ (Wilson and Fred), 503.
Parallelism, remarkable (Goldschmidt), 219.
Paramecium Aurelia (Sonneborn), 378; (Kimball), 469.
PARKER, G. H. Color Changes Due to Erythrophores in the Squirrel Fish, Holocentrus, 206.
——. Antagonism in Neurohumors as Seen in the Pectoral Bands of Mustelus, 596.
——. Antidromic Responses from the Melanophore Nerves of the Catfish Ameiurus, 595.
Parthenogenesis, haploid (Cooper), 41.
Partition function (Rademacher), 78.
PASTERNACK, S. On the Mean Value of $r^s$ for Keplerian Systems, 91, 250.
Patagonia (Berry), 537.
PAULING, L., AND STURDIVANT, J. H. The Structure of Cyameluric Acid, Hydromelonic Acid and Related Substances, 615.
Peccary skull (Stock), 398.
Phenols, substituted (Tyler and Horowitz), 369.
Phosphorus (Scott and Cook), 265.
Phosphorus, radio (Cook, Scott and Abelson), 528.
Phycomyces, growth of (Robbins and Kavanagh), 499.
Pigments, lipoid-soluble (Fox), 295.
Pisces (Zwicky), 251.
Plant embryos (Bonner and Axtman), 453.
Plate rows (Coonfield), 152.
PLOUGH, H. H., AND CHILD, G. P. Autosomal Lethal Mutation Frequencies in Drosophila, 435.
Polymorphic transitions (Bridgman), 202.
Polynomials, approximation by (Sewell), 491.
Populations (Wright), 307.
Potential barriers (Muskat and Hutchisson), 197.
POULSON, D. F. Chromosomal Deficiencies and the Embryonic Development of Drosophila Melanogaster, 133.
Prediction-accuracy (Laughlin), 60.
Prehistory, Puerto Rican (Rouse), 182.
Products in a complex (Whitney), 285.
Projective geometry (Michal), 546.
Psychophysics of hearing (Upton and Holway), 29, 32.
Puerto Rican prehistory (Rouse), 182.
Puparium-formation (Hadorn), 478.
Pyrimidine (Robbins, Bartley, Hogan and Richardson), 388.

RADEMACHER, H. A Convergent Series for the Partition Function $p(n)$, 78.
Radiative gradients (Chandrasekhar), 572.
Radioactive phosphorus (Scott and Cook), 256.
Radio-biological reactions (Nurnberger), 189.
Radio disturbances, interstellar (Whipple and Greenstein), 177.
Radio phosphorus, deposition of (Cook, Scott and Abelson), 528.
Radio-sodium absorption (Hamilton), 521.
Rat, linkage in (King and Castle), 56.
RAWLES, M. E. See Willier, B. H., 542.
Reactions, radio-biological (Nurnberger), 189.
Real numbers, transfinite (Gleyzal), 581.
Regeneration of plate rows (Coonfield), 152.
REISSNER, M. E. On the Theory of Beams Resting on a Yielding Foundation, 328.

Representations of algebras (Brauer and Nesbitt), 236.
Representations in a subgroup (Clifford), 89.
Representations, irreducible (Murnaghan), 277, 488.
Responses, antidromic (Parker), 595.
RICHARDSON, L. R. See Robbins, W. J., 388.
"Ring-glands," normal (Hadorn), 478.
Rings, continuous (v. Neumann), 341.
ROBBINS, W. J., AND BARTLEY, M. A. Thiazole and the Growth of Excised Tomato Roots, 385.
ROBBINS, W. J., BARTLEY, M. A., HOGAN, A. G., AND RICHARDSON, L. R. Pyrimidine and Thiazole Intermediates as Substitutes for Vitamin $B_1$, 388.
ROBBINS, W. J., AND KAVANAGH, F. Intermediates of Vitamin $B_1$ and Growth of Phycomyces, 499.
Roots (van Overbeek), 272.
ROSENTHAL, J. E., AND MOTZ, L. Application of a New Mathematical Method to Vibration-Rotation Interaction, 259.
ROUSE, I. New Evidence Pertaining to Puerto Rican Prehistory, 182.

Salivary gland (Buck), 423.
Sciara (Buck), 423.
SCOTT, K. G., AND COOK, S. F. The Effect of Radioactive Phosphorus upon the Blood of Growing Chicks, 265.
SCOTT, K. G. See Cook, S. F., 528.
Seeds and X-rays (Bless), 194.
Semi-group (Vandiver), 552.
Seminal vesicles (Young and Fox), 461.
SETCHELL, W. A., AND GARDNER, N. L. Iridophycus in the Northern Hemisphere, 169.
SEWELL, W. E. Degree of Approximation by Polynomials—Problem $\alpha$, 491.
Sex characters (Witschi), 35.
Sex, inheritance of (Kimball), 469.
Sex, inheritance and determination (Sonneborn), 378.
Sex-ratio (Sturtevant), 360.
SHAPLEY, H. A Survey of Thirty-Six Thousand Southern Galaxies, 449.
SINNOTT, E. W. The Relation of Gene to Character in Quantitative Inheritance, 224.
Skin transplants (Willier, Rawles and Hadorn), 542.
Skull, peccary (Stock), 398.
SLOBUTSKY, C., AUDRIETH, L. F., AND CAMPBELL, R. W. Acid Catalysis in Liquid Ammonia. I. Ammonolysis of Diethylmalonate, 611.
SNELL, G. D., AND AEBERSOLD, P. C. The Production of Sterility in Male Mice by Irradiation with Neutrons, 374.
SONNEBORN, T. M. Sex, Sex Inheritance and Sex Determination in Paramecium Aurelia, 378.
South Africa, Corallines (Manza), 568.
Southern galaxies (Shapley), 449.
Spaces, bicompact (Wallman), 164.
Spaces, linear topological (Hyers), 496.
Spaces, non-compact (Dowker), 293.
Species, evolution of (Kinsey), 5.
Spectroscopic absolute magnitudes (Hoffleit), 111.
Spindle attachment in X-chromosome (Tan), 351.
Squirrel fish (Parker), 206.
Stars, interiors of (Chandrasekhar), 572.
Stars, magnitudes of (Hoffleit), 111.
Stars, variable (Sterne and Campbell), 115.
Statistical theory of turbulence (von Kármán), 98.
Stearic acid (Germer and Blodgett), 390.
STEINBERG, A. G. Relations between Chromosome Size and Effects of Inversions on Crossing-Over in Drosophila Melanogaster, 54.
Sterility in male mice (Snell and Aebersold), 374.
STERNE, T. E., AND CAMPBELL, L. Changes of Period in Variable Stars of Long Period, 115.
Stieltjes transform (Widder), 242.
Stimuli, visual (Sumner and Doudoroff), 211.
STOCK, C. An Eocene Titanothere from San Diego County, California, with Remarks on the Age of the Poway Conglomerate, 48.
——. A Peccary Skull from the Barstow Miocene, California, 398.
STORKS, K. H. See Germer, L. H., 390.
Strength-duration (Crozier), 71.
Structure of cyameluric acid, hydromelonic acid and related substances (Pauling and Sturdivant), 615.
STURDIVANT, J. H. See Pauling, L., 615.
STURTEVANT, A. H. An Effect of the Y-Chromosome on the Sex-Ratio of Inter-Racial Hybrids of Drosophila Pseudoöbscura, 360.
Subgroup, invariant (Walsh), 89.
Subjective tones (Lewis and Larsen), 415.
SUMNER, F. B., AND DOUDOROFF, P. Some Quantitative Relations between Visual Stimuli and the Production or Destruction of Melanin in Fishes, 211.
Superfemales in Drosophila Melanogaster (Beadle and Ephrussi), 356.
Supraconductors (Epstein), 604.
Symbiotic nitrogen fixation (Wilson and Fred), 503.
Symmetric group (Murnaghan), 277, 488.

TAN, C. C. Compressed Deficiency and the Location of the Spindle Attachment in the X-Chromosome of Drosophila Pseudoöbscura, 351.

Thiazole (Robbins and Bartley), 385; (Robbins, Bartley, Hogan and Richardson), 388.
THIMANN, K. V., AND BEADLE, G. W. Development of Eye Colors in Drosophila: Extraction of the Diffusible Substances Concerned, 143.
Threshold, visual (Hecht), 227.
Tissue culture (Tukey), 577.
Tissue, haploid ovarian (MacKnight), 440.
Titanothere, Eocene (Stock), 48.
Tomato roots (Robbins and Bartley), 385.
Tones, subjective (Lewis and Larson), 415.
Topological spaces, linear (Hyers), 496.
Transfinite real numbers (Gleyzal), 581.
Transform, Fourier (Condon), 158.
Transform, Stieltjes (Widder), 242.
Transformations, transitive (Oxtoby), 443.
Transitions, polymorphic (Bridgman), 202.
Transmission coefficients (Muskat and Hutchisson), 197.
Transplants, ovary (Beadle and Ephrussi), 356.
Transplants, skin (Willier, Rawles and Hadorn), 542.
Trihornometry (Kasner), 337.
TUKEY, H. B. Plant Parts of Deciduous Fruits Which Give Evidence of Being Favorable for Tissue Culture, 577.
Turbulence, statistical theory of (von Kármán), 98.
TYLER, A., AND HOROWITZ, N. H. The Action of Certain Substituted Phenols on Marine Eggs in Relation to Their Dissociation, 369.

UPTON, M., AND HOLWAY, A. H. On the Psychophysics of Hearing. I. Monaural Differential Sensitivity and Exposure-Time, 29.
——, ——. On the Psychophysics of Hearing. II. Binaural Differential Sensitivity and Exposure-Time, 32.

VANDIVER, H. S. On the Concept of Co-Sets in a Semi-Group, 552.
——. On Generalization of the Numbers of Bernoulli and Euler, 555.
Variable stars (Sterne and Campbell), 115.
Vesicles, seminal (Young and Fox), 461.
Vibration-rotation interaction (Rosenthal and Motz), 259.
Visual excitation (Crozier, Wolf and Zerrahn-Wolf), 516.
Visual stimuli (Sumner and Doudoroff), 211.
Visual threshold (Hecht), 227.
Vitamin $B_1$ (Robbins, Bartley, Hogan and Richardson), 388, 499.

WALLMAN, H. Lattices and Bicompact Spaces, 164.
WALSH, J. L. Note on the Curvature of Level Curves of Green's Function, 84.
——. Note on the Curvature of Orthogonal Trajectories of Level Curves of Green's Function, 166.
WELSH, J. H. The Eye-Stalk Hormone and Rate of Heart Beat in Crustaceans, 458.
WHIPPLE, F. L., AND GREENSTEIN, J. L. On the Origin of Interstellar Radio Disturbances, 177.
WHITNEY, H. On Products in a Complex, 285.
WIDDER, D. V. The Iterated Stieltjes Transform, 242.
WILLIER, B. H., RAWLES, M. E., AND HADORN, E. Skin Transplants between Embryos of Different Breeds of Fowl, 542.
WILSON, P. W., AND FRED, E. B. Mechanism of Symbiotic Nitrogen Fixation. II. The $pO_2$ Function, 503.
WITSCHI, E. Stimulative and Inhibitive Induction in the Development of Primary and Secondary Sex Characters, 35.
WOLF, E. See Crozier, W. J., 516.
WRIGHT, S. The Distribution of Gene Frequencies in Populations, 307.

X-chromosome (Tan), 351.
X-rays and chromosomes (Marshak), 362.
X-rays, genetic affects (Fricke and Demerec), 320.
X-rays and seeds (Bless), 194.

Y-chromosome (Sturtevant), 360.
YIN, H. C. Effect of Auxin on Chlorella Vulgaris, 174.
YOUNG, R. T., AND FOX, D. L. The Seminal Vesicles of the Goby with Preliminary Chemical and Physiological Studies of the Vesicular Fluid, 461.

ZARISKI, O. Some Results in the Arithmetic Theory of Algebraic Functions of Several Variables, 410.
ZERRAHN-WOLF, G. See Crozier, W. J., 516.
ZWICKY, F. Intrinsic Properties of Light and Corpuscles from Distant Sources, 106.
——. On a New Cluster of Nebulae in Pisces, 251.